Health Protection and Drug Laws

Health Protection and Drug Laws

Health and Welfare Canada
Santé et Bien-être social Canada

Health Protection and Drug Laws

Educational Services
Health Protection Branch
Department of National Health and Welfare

Published by authority of the
Minister of National Health and Welfare
2/80

Available in Canada through

Authorized Bookstore Agents
and other bookstores

or by mail from

Canadian Government Publishing Centre
Supply and Services Canada
Hull, Quebec, Canada K1A 0S9

Catalogue No. H49-5/1980E
ISBN 0-660-10264-1

Canada: $2.95
Other countries: $3.60

Price subject to change without notice.

Contents

Introduction

Two acts form the basis of the drug laws: the *Food and Drugs Act* and the *Narcotic Control Act*. The responsibility for administering these acts rests mainly with the Health Protection Branch, Department of National Health and Welfare (see the chart reflecting the various drug responsibilities of the Branch).

Why have drug laws? What are the drug laws? How are these laws implemented? It is the purpose of this publication to answer these three questions. The answers are directed mainly at health professionals, students in the health professions, consumer advocate groups, and students of consumer protection laws. It is hoped that this publication will be useful in their dealings with the general public, the government, and industry.

Because the volume of legislation that can be outlined in this type of publication is limited, the reader who wants more detail may use this guide in conjunction with the Acts and Regulations and may also refer to the source material listed in the bibliography at the end of each chapter.

A glossary of terms is included at the end of the booklet.

Chapter 1
Perspective

Evolution of The Drug Laws

Laws are a means of ensuring that drugs are safe and effective and are being used wisely. The acts that detail these laws, the *Food and Drugs Act* and the *Narcotic Control Act,* evolved from different pieces of legislation.

Food and Drugs Act

Inland Revenue Act (1875)
Dealt mostly with the adulteration of alcohol; drugs not defined. Forerunner of more effective legislation.

Adulteration Act (1884)
Defined drug, adulteration, and conditions under which adulteration might take place.

Repealed

Food and Drugs Act (1920)

Food and Drugs Act (1953)
Controls manufacture, distribution, and sale of drugs except narcotics. Drugs formerly listed under PPM Act are now governed by this Act.

Proprietary or Patent Medicine Act (1909) Passed because of concern over efficacy and safety of secret-ingredient drugs.

Revoked
1977

Narcotic Control Act

Opium Act (1908)
Prohibited the unauthorized importation and possession of gum or smoking opium.

Opium and Drug Act (1911)
Included other problem drugs, e.g. cocaine and morphine.

Opium and Narcotic Control Act (1920)
Illicit trade in narcotics was increasing; more control necessary.

Narcotic Control Act (1961)
Controls the manufacture, distribution, and sale of narcotic drugs.

The Regulations

The Acts contain broad statements relating to safety and efficacy. The more detailed technical requirements are outlined in the Regulations.

The Regulations are also a means of rapidly updating legislation; they have the same force and effect as the Act itself.

Requests for changes arise from many sources: the government, professional or trade organizations, consumer groups, and industry. When identifying the need for new or changed regulations, the Branch considers such subjects as health hazards, fraud, surveillance problems, and international standards. Proposed changes are communicated to the drug industry, health professionals, and consumers by means of the *Information Letter,* distributed by the Health Protection Branch. Comments submitted by these concerned parties is considered in the drafting of new legislation.

The proposed regulation is reviewed by the Minister of National Health and Welfare, and if the Minister agrees, it is presented to the Governor-in-Council (a committee of the Cabinet) for passage. When passed, it is published in the *Canada Gazette*, Part II, which is issued twice monthly and contains all new and amended federal regulations.

Branch Communications

The Health Protection Branch (HPB) maintains constant contact with the drug industry and various professional and consumer groups. Such communications are vital for mutual understanding of roles and concerns and for obtaining the best possible advice in the development of new policies and regulations.

A continuing liaison is maintained with many professional organizations in such fields as pharmacy, medicine, dentistry, and veterinary medicine. Experts from these organizations are invited to sit on committees to advise the Branch on contentious or developing issues. For example, the Committee on Reproductive Physiology provides recommendations to the Branch relating to physical or chemical alterations of normal and abnormal reproductive physiology in males and females. The recommendations of the Committee have resulted in modifications of some products containing estrogens, addi-

tional label warnings on others, a revision of the patient package insert for oral contraceptives, and the discontinuance of the sale of some oral contraceptives, including the sequentials.

The Branch also maintains contact with national organizations concerned with specific diseases (e.g. arthritis, cancer, diabetes) and consumer groups through its central office in Ottawa and its five regional offices across Canada.

Bibliography

Morrison, A. B. 1975. The Canadian approach to Food and Drug Regulations. *Food, Drug, Cosmetic Law Journal* 30: 632-643.

Pugsley, L. I. 1967. The administration and development of federal statutes of foods and drugs in Canada. *Medical Services Journal, Canada* 23 (3): 387-449.

Prepared by and available from Educational Services:

Old Visions — New Beginnings — booklet

Canadian Drug Laws and the Consumer — *Dispatch* No. 33

The Canadian Food and Drugs Act and Regulations and the Narcotic Control Act and Regulations may be purchased from
Department of Supply and Services
Publishing Centre
Hull, Québec K1A 0S9

Chapter 2
Drugs and their availability

> *A drug is any substance used in the diagnosis, treatment, mitigation, or prevention of a disease, disorder, or abnormal physical state, and in restoring, correcting, or modifying organic functions, in man or animals.* (Paraphrased from the Food and Drugs Act)

Availability of drugs is governed by considerations of safety and effectiveness, i.e. the potential for misuse and the amount of professional consultation needed. At one end of the spectrum are drugs such as A.S.A. (acetylsalicylic acid) that may be bought in a grocery store by any person; at the other end are drugs such as LSD (lysergic acid diethylamide) that may be obtained legally only by a research institution with an authorization from the Minister of National Health and Welfare. The former can provide relief from a minor headache, easily self-diagnosed; the latter has no known medicinal use.

The health professional — physician, dentist, pharmacist, nurse, veterinarian — plays an important role in monitoring the availability of drugs to the general public. The amount of involvement depends on safety considerations. Federal laws provide many of the guidelines on availability, but provincial laws may further restrict the availability of a drug. The practice of pharmacy is regulated provincially.

Vaccines, Sera, Radiopharmaceuticals, Antitoxins

Drugs such as these are administered by a physician or a nurse, when required. The patient does not normally have access to these drugs, except through the physician.

Over-the-Counter preparations (OTCs)

These are drugs that do not require a prescription. There are two basic categories of OTCs. One group contains those preparations used for treatment of minor, self-limiting illnesses, which generally do not require the advice or intervention of health professionals. The other group is made up of medicines that, although they do not require a prescription, may require professional advice before they are used.

The first category includes many of the more common remedies such as antacids, laxatives, minor pain-relievers, headache remedies, cough and cold medicines, sinus and nasal preparations, and most vitamin preparations. Most drugs are usually sold in pharmacies. However, this category includes the proprietary medicines, most of which can be bought in non-pharmacy outlets. Proprietary medicines are drugs that were formerly regulated by the Proprietary or Patent Medicine Act.

The second category is made up of a wide range of pharmaceuticals which are not restricted by prescription but are usually kept behind the counter. Some examples of drugs in this area are insulin and nitroglycerin. Because

of the very nature of the conditions they treat, they require initial and extensive consultation with a physician. The user is trained and practised in the self-administration of the drug. Other examples of such drugs are some muscle relaxants and antispasmodics, and therapeutic vitamins. Many of the drugs in this category are prescribed or recommended by medical practitioners for long-term use.

Drug or cosmetic?

Some products may be perceived by the general public to be cosmetics, but because they alter bodily functions are by definition drugs and are regulated as such (all are OTCs).

e.g.

- . A toothpaste is a cosmetic when it cleans, whitens, and brightens the teeth; it is a drug when an ingredient, such as fluoride, is added to help prevent tooth decay.
- . A deodorant is a cosmetic because it masks odor in perspiration; an antiperspirant is a drug because it suppresses the flow of perspiration.

Federal vs. provincial laws

Some drugs are OTCs federally but prescription drugs provincially. For example

British Columbia	ephedrine and its salts (for internal use containing ephedrine as the single active ingredient)
Ontario	digitalis, its glycosides or derivatives

Prescription Drugs

Many drugs are available to the general public only after consultation with a medical practitioner (a physician or dentist) and the presentation of a prescription to a registered pharmacist. A prescription is an order given by a practitioner directing that a stated amount of a drug be dispensed for the person named in the order.

The main reasons for requiring additional control for these drugs are the need for professional direction and supervision in their use and in some cases their potential for abuse or misuse.

Types of prescription drugs are listed below; they are categorized according to the extent of control necessary for their safe use.

Vitamins A and D

Although usually sold as OTCs, preparations of vitamins A and D require a prescription when the maximum daily dose recommended on the label exceeds 10 000 and 1000 IU, respectively. Large doses of such vitamins can be toxic.

Schedule F drugs Pr

More than 200 drug substances are listed in Schedule F to the Food and Drug Regulations and represent a wide diversity of classes, such as antibiotics, hormones, and tranquilizers. Schedule F, perhaps more than any other, is subject to frequent changes. These result from the discovery and introduction to the marketplace of new drug substances, the identification of hazards of certain OTCs, and knowledge of changing abuse and misuse patterns.

The symbol [Pr] must appear on labels of these drugs.

Controlled drugs ◇C

At present about 12 drugs are classified as controlled drugs and are listed in Schedule G to the Food and Drugs Act. They are stimulants (e.g. amphetamines, methamphetamines) and sedatives (e.g. barbituric acid, methaqualone).

The symbol ◇C must appear on labels and all professional advertisements.

One of the effects of amphetamines, methamphetamines, phendimetrazine, and phenmetrazine is the depression of appetite; thus these drugs became popular in the treatment of obesity. Because these drugs have a mood-modifying effect and can be habit-forming, they created more serious problems than the condition they were being used to treat. Hence, they are now also referred to as "Designated Drugs" and can only be prescribed for the following conditions:

Humans	narcolepsy, hyperkinetic disorders in children, mental retardation (minimal brain dysfunction), epilepsy, parkinsonism, hypotensive states associated with anesthesia
Animals	depression of cardiac and respiratory centres

Narcotic drugs "N"

Narcotic drugs are controlled by the Narcotic Control Act and Regulations and are listed in the Schedule to that Act. Examples of drugs in this group are cocaine, opium, codeine, morphine, phencyclidine, and cannabis (marijuana).

Some of these drugs have a legitimate medicinal use such as the relief of pain. However, their psychotropic effects (ability to modify mental activity) and addictive properties have led to stringent restrictions on their availability.

The letter "N" must appear on all labels and professional advertisements.

Codeine: the only narcotic preparations that can be sold to the general public without a prescription are oral preparations of codeine phosphate or its equivalent in concentrations not more than
8 mg/tablet or other solid form
20 mg/28mL
(Section 27, Narcotic Control Regulations).
Such products must also contain at least two additional medicinal ingredients (e.g. A.S.A., pheniramine maleate) in specified proportions.

Restricted Drugs

These substances, which have hallucinogenic properties (alter perception from objective reality with serious physiological and psychological effects), have no recognized medicinal use and are dangerous. There are about 23 such chemicals, which are listed in Schedule H to the Food and Drugs Act. The most well known is lysergic acid diethylamide (LSD). These chemicals are only available to institutions involved in highly specialized research. An authorization is required from the Minister of National Health and Welfare before such a drug can be sold.

Veterinary Drugs

Drugs listed in Part I of Schedule F to the Food and Drug Regulations may be sold only on prescription, whether for human or veterinary use. A prescription is not required for drugs listed in Part II, provided they are in a form that can only be used for animals or are labelled that they are for agricultural use only.

Drug residues in food

Such residues can have serious health consequences in terms of toxicity and allergic responses in sensitive individuals. To minimize this risk the labels of most veterinary drugs used in food-producing animals must specify the withdrawal period, i.e. the time between the last treatment of the drug and the use of the animal for food, either by slaughtering or the collection of milk or eggs. This period must elapse to ensure that residues of the drugs have been eliminated from any edible products derived from the animal.

Any antibiotic that leaves traces in the milk of lactating cattle longer than 96 hours after administration must not be used for their treatment. Also, different antibiotics are found in Parts I and II of Schedule F. Those found in Part I are more likely to persist in food and therefore require the additional control of a prescription when being used for animals.

Medicated animal feeds

These commodities are a shared concern between Health Protection Branch and Agriculture Canada. Information on the use of medicated animal feeds is contained in Agriculture Canada's *Compendium of Medicating Ingredients Brochures*, which specifies the drugs, their dosages, and the indications and conditions of use applicable to the manufacture and sale of registered medicated feeds. Only drugs that comply with the Food and Drugs Act and are listed in the *Compendium* are eligible for registration by the Department of Agriculture.

Bibliography

Curran, R. E. 1953. *Canada's Food and Drugs Laws*. Commerce Clearing House Inc, Chicago, Ill.

Food and Drugs Act and Regulations, with Amendments to June 1978.

Health and Welfare Canada. 1974. Investigation of use and reason for use of non-prescription drugs. *Report D. National Purchase Diary*. C. H. and Z Limited, Toronto.

Narcotic Control Act and Regulations, with Amendments to May 26, 1977.

Prepared by Educational Services:
*Over-the-counter remedy series — folders

Antacids
Cough Remedies
The Laxative Habit
Vitamin Preparations

*Antibiotics — Handle with Care — *Dispatch* No. 11
Pain Relievers for Self Medication — *Dispatch* No. 28
Second Report on Oral Contraceptives — *Dispatch* No. 35
Cosmetic Safety and the Consumer — *Dispatch* No. 40
*The Cost of Tranquility — *Dispatch* No. 42

** Available from the Health Services and Promotion Branch, Health and Welfare Canada.*

Chapter 3
Record Keeping and the Prescription

Prescriptions for all Schedule drugs must be retained by a pharmacist for a minimum of two years. A verbal prescription must be recorded in writing and the pharmacist must be satisfied that the source of the verbal order is legitimate.

Prescriptions for Schedule drugs must include the following information:

- date and number of prescription;
- name and address of person for whom the prescription is written;
- name and quantity of drug specified by the practitioner;
- name of person filling prescription and name of the practitioner who prescribed it;
- directions for use given with the prescription, including the number of times, if any, it can be refilled.

Refills are only permitted on authorization of a practitioner. Each time a prescription is refilled the following information must be recorded on the original prescription or in a suitable patient record system:

- quantity of drug dispensed,
- date of refill,
- name of the person refilling the prescription.

A narcotic prescription may not be refilled — a new and separate prescription from a practitioner is required.

Bibliography

Food and Drug Regulations, with Amendments to October 1979 (Sections C.01.041 — C.01.042).

Chapter 4
New Drugs

Any drug that has not been sold in Canada for sufficient time and in sufficient quantity to establish in Canada its safety and effectiveness under the use or conditions of use recommended is defined as a new drug in the Regulations.

Research

It has been estimated that chemists create or isolate up to 5000 chemical substances to arrive at one new marketable drug. After isolation and purification, a new compound will be administered either to tissue cultures or to small animals to see whether there are significant physiological or behavioural changes (whole animals) or morphological or biochemical changes (tissue cultures). This indicates that the drug is active and may thus be useful in reversing pathophysiology of diseased states in man or animal. If promising results are obtained for the compound, preclinical animal studies are initiated.

Preclinical Testing

Preclinical animal studies

Initially the nontoxic to lethal dosage ranges of the compound are determined in tests conducted on non-diseased animals of at least three mammalian species (one must be a non-rodent). If the substance seems to be of potential therapeutic value for human use, more detailed studies are undertaken; these may take several years to complete. If results are positive, the manufacturer may then apply to the HPB for permission to conduct a clinical (i.e. human) pharmacology trial by a qualified investigator.

Clinical pharmacology trial

The compound is administered to healthy human volunteers, building gradually to the predicted effective dose to see whether any unpredicted adverse or toxic symptoms occur. At the same time, the manufacturer is assessing the requirements for large-scale production of the compound.

Production methods and quality control procedures must be designed to ensure a relatively pure compound essentially free of contamination and uniform with respect to all quality aspects. The compound must be stable in its dosage form for a reasonable period of time to permit the clinical investigations to proceed. If any of these factors are unfavourable, measures must be taken to improve them before the compound progresses to clinical trials.

Clinical Trials

The manufacturer files a preclinical new drug submission with the Drugs Directorate requesting permission to distribute the drug to named, qualified investigators, for more extensive testing to determine the new drug's dosage, effectiveness, and safety in treating humans.

The information submitted must include all testing on humans and/or animals done up to this time. In addition, since the method of manufacture may affect the efficacy and safety of a drug, information on the manufacturing methods, standards, and stability of the drug substance and dosage form must be present, so that the product that may eventually be sold to the public has the same composition as that determined to be effective and safe in the

clinical trials.

The investigator is subject to comprehensive regulations because at this point, testing is being carried out on persons with the disease state or condition that the compound is expected to treat; the results are compared with other drugs or methods of treatment used for the same condition. If clinical studies prove that the new drug has therapeutic value, the manufacturer may then file a new drug submission.

The New Drug Submission

Before marketing a new drug, a manufacturer must file a new drug submission with the Branch and receive a notice of compliance.

The new drug submission contains virtually all information known about the drug and results of studies carried out on the drug substance and the dosage forms available. Information about the drug substance includes its proper name, chemical name(s), details of the method of manufacturing and purification; and its physico-chemical, biological, pharmacological, pharmacodynamic, and pharmacokinetic properties. Information about the dosage form includes quantitative listing of all ingredients used in the formulation, its method of manufacture, packaging, labelling, results of stability tests, therapeutic claims, side effects, as well as details of clinical studies to support the safety and efficacy of the drug. The submissions themselves range in size from a few pages to several hundred volumes. Samples of the market-ready form of the new drug are also received with the submission for possible analytical testing.

Review and Evaluation

All aspects of the submission are critically reviewed by multidisciplinary teams of the Drugs Directorate. The final reviews deal with the wording of the product monograph, which provides all information on the drug and complete prescribing instructions to physicians. When the new drug submission is found satisfactory, the labels are examined and a *notice of compliance* is issued permitting the manufacturer to sell his product.

Marketing Controls

Once a new drug is on the market, controls do not cease. It may remain in a new drug status for a number of years until the Drugs Directorate is confident that sufficient information has been accumulated from its general use to release it from the rigid controls that are applied to all new drugs. The manufacturer must report any new information he receives concerning side effects or failure on the part of the drug to produce its desired effect. On request, the manufacturer is required to notify the Drugs Directorate about any animal tests that have provided new information. A notice of compliance for a new drug can be suspended; under these circumstances the drug is removed from the market if this is in the interest of public health.

Bibliography

Food and Drug Regulations,
with Amendments to October 1979.
(Section C.08.001).

Health and Welfare Canada.
1965. *Guide for Completing Preclinical Submissions on Investigational Drugs*
(available from HPB, Bureau of Drugs).

Prepared by and available from
Educational Services:
The Marketing of a New Drug —
Dispatch No. 24

Chapter 5
Drug Standards

Most single-ingredient drugs are manufactured to standards contained in the publications listed in Schedule B to the Food and Drugs Act:

Pharmacopée Française (Ph.F)
Pharmacopoeia Internationalis (Ph.I.)
British Pharmacopoeia (B.P.)
The Pharmacopeia of the United States of America (U.S.P.)
The Canadian Formulary (C.F.)
The British Pharmaceutical Codex (B.P.C.)
The National Formulary (N.F.)

For some special single-ingredient drugs specific requirements are set out in the Regulations, e.g. insulin.

Drugs listed in Schedule B publications or in the Regulations (Division 6, Part C) are known as *official drugs*.

A *manufacturer's standard* ("house" standard) may be used by a manufacturer for any drug listed in Schedule B publications so long as the most stringent criteria set out for purity and potency in these publications are met.

A *professed standard* may be established by a manufacturer for any drug for which there is no standard in the Regulations or in any Schedule B publication. Such standards are necessary for many single-ingredient products, including many new drugs, and for most multiple-ingredient products. In the case of the latter, many individual components will have to meet pharmacopoeial standards, but the final product will have to meet the standard established by the manufacturer.

What is a Standard?

A "typical" standard may include a physical and chemical description of the drug entity, a description of procedures for identification, the permitted pH range, tests for heavy metals, pyrogen and sterility requirements for parenteral preparations, assay methods and procedures, packaging and storage requirements, and any special label instructions for the user of the drug.

Some Legislated Drug Specifications

- Compressed tablets that are intended to be swallowed whole must disintegrate within 60 minutes, under specified test conditions. This requirement is designed to ensure that the tablet will not pass whole through the digestive system.
- Enteric coated tablets are formulated to release their ingredients in the upper small intestine after passage intact through the stomach. A test ensures that they do not disintegrate in an acid medium such as is found in the stomach, but do so within 60 subsequent minutes in an alkaline medium similar to that of the upper small intestine.
- Safety factors such as sterility and the absence of pyrogens must be assured in parenteral drugs.

Chapter 6
Advertising/Labelling/Packaging

No person shall label, package, treat, process, sell or advertise any drug in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety.
(Subsection 9(1) Food and Drugs Act)

Labelling

The label of a drug product is one of the most important sources of drug information available to the consumer and health professional.

In addition to the commonly understood meaning of "label," any literature accompanying or belonging to a particular drug product is considered to be labelling material. An inner label is that on an immediate container; an outer label is that on the outside of a drug package.

Basic information must appear on the label:

- proper name of a drug or if there is no proper name, the common name;
- name and address of the manufacturer or distributor of the drug;
- lot number (a means by which a drug can be traced in manufacture and identified in distribution);
- quantitative list of medicinal ingredients by their proper or common names;
- DIN or GP number assigned to the drug (see Chapter 8);
- expiration date for certain specified types of products and for all others that do not maintain potency, purity, and physical characteristics for at least three years from date of manufacture;
- net content (on outer label or if there is only one label, on that label);
- adequate directions to promote the wise use of the drug (e.g. purpose and dosage of drug, route of administration, cautions, warnings, contra-indications);
- standard to which the drug is manufactured (see Chapter 5).

If there is insufficient space on the inner label to carry all the required information, some of it may be supplied on a package insert. The inner label should refer to the inclusion of a package insert.

Labels of drugs bought on prescription

Provincial legislation usually specifies what must appear on the label of a drug that is sold on prescription. Those involved in prescribing and dispensing the drug are expected to provide the necessary guidance and warnings so that the drug is properly taken. This information may be communicated by the pharmacist and physician verbally or in written form.

Proper name

This is the name assigned the drug in publications listed in Schedule B to the Food and Drugs Act, or in the Regulations. The proper name usually differs from the chemical name, e.g. acetaminophen is the proper name for *N*-acetyl-*p*-aminophenal.

Recommended dosage

To ensure safe and effective use of a drug, all labels must carry a recommended single or daily dosage or dosage range. For some OTCs this dosage is limited by legislation (Table of Limits of Drug Dosage, C.01.021) and may only be exceeded if the label bears a caution that a physician should be consulted; a reduced dosage must be stated when these drugs are recommended for children.

Net content

This is the net amount of the drug in terms of weight, measure, or number. When A.S.A. is in a dosage form recommended only for children, the package may not contain more than 24 single doses.

Children and label precautions

- Codeine-containing compounds sold without a prescription must carry the warning not to administer to children except on the advice of a physician.
- A.S.A. must carry a warning on the label that the substance must be kept out of reach of children. A red octagon must be used to call attention to the warning.
- Preparations containing boric acid or sodium borate must caution against administration to infants and children under the age of three years.

Disposable pressurized containers

The label must call attention to the potential hazards inherent in this type of packaging. The statement "contents under pressure" must appear on the label.

If the contents are very flammable (flash point less than 65°C) then statements referring to this must appear on the label.

This symbol must appear on the main panel.

This symbol must appear on the main panel if the contents are very flammable.

Radiopharmaceuticals
Outer labels must bear a licence number (see Chapter 10), a radiation warning symbol (☢), and the statement "caution — radioactive material."

Storage instructions
These instructions are necessary to

- maintain the potency and to prevent degradation of ingredients,
- protect the user from dangers inherent in the packaging, as in the case of the aerosol container.

e.g.

- Store at room temperature.
- Keep refrigerated.

Vitamins and minerals

- When certain disease states or deficiencies require a high intake of specified vitamins and minerals, products are permitted to contain more than the maximum level of the nutrient specified in the vitamin and mineral regulations for most OTC products. Such products must be clearly labelled "for therapeutic use only" and should be used only on the advice of a physician.
- Labels of all vitamin preparations must carry an expiry date.

Veterinary drugs

- Labels of drugs listed in Part II of Schedule F to the Food and Drug Regulations when sold without a prescription for use in animals must say "for agricultural use only" or "for veterinary use only."
- Labels of most veterinary drugs used in food-producing animals must specify the withdrawal period for the drug (see Chapter 2).

Schedule A diseases
Claims for Schedule A diseases (Appendix I) may not be made on the label except where it is necessary for the safe use of a parenteral (e.g. insulin) or a prescription drug.

Label monitoring
The Bureau of Drug Surveillance conducts an ongoing monitoring program to assess the manufacturer's compliance with labelling regulations.

Advertising

For the following classes of drugs, professional advice is required for the proper diagnosis and treatment of a disease or condition, or for the administration of the drug. Thus advertising to the *general public* is prohibited for

- narcotic drugs;
- controlled drugs;
- drugs in Part I of Schedule F (to the Regulations) except for name, price, and quantity;
- OTCs that have limits for recommended dosages (as specified in the Table of Limits of Drug Dosage, C.01.021) when these limits are exceeded, e.g. A.S.A. in amounts greater than 975 mg/single dose or 2.925 g/day;
- drugs for treatment of Schedule A diseases (Appendix I);
- vitamins labelled "for therapeutic use only";
- minerals labelled "for therapeutic use only".

Health professionals and drug advertising
The above restrictions have been developed for the protection of the lay pub-

lic. They do not apply to advertising directed to health professionals. Such factors as new developments in the field of medicine and treatments for Schedule A diseases are valuable to medical practitioners and of assistance to them in assessing the risk/benefit ratio of treatments.

"False, misleading or deceptive or is likely to create an erroneous impression"
Subsection 9(1) Food and Drugs Act

The above is interpreted to be advertising that

- contradicts current medical or scientific knowledge,
- cannot be supported by clinically valid and statistically reliable data,
- contains confusing or misleading words and phrases,
- gives an overall inaccurate impression.

Some words that may be misleading:

- natural, natural source, natural action
  few drugs are so devoid of processing as to justify the descripion "natural"; drugs of vegetable origin obtained with minimum processing may be described as "natural source"; "natural action" should not be used as all drugs act by artificially stimulating or assisting bodily functions.
- organic
  no meaning, as many drugs may be defined chemically as organic compounds.

Some unacceptable promotion methods:

- product endorsements
  including professional endorsements, quotations from the media, seals or certificates of approval and testimonials.
- comparisons
  these are often incomplete in that they frequently highlight only the advantages of the advertised product and the disadvantages of the competitor's product; they often emphasize product differences which have little or no significance.
- negative statements
  e.g. to say a particular product is non-toxic implies that comparable products may be toxic.
- scientific or technical references
  the consuming public does not generally have sufficient expertise to assess the validity of such references.

Children and drug advertising
Drug advertising should not be directed towards children, as this may encourage unsupervised use of drugs by children and could establish drug-taking habits early in life. Therefore, drug advertisements such as the following are unacceptable:

- those that portray children discussing drug products or requesting a certain drug;
- those that place more stress on a premium being offered than on the health reason for taking a drug;
- those that exaggerate aspects of a product that would appeal to

children, e.g. by portraying drug taking as fun or grown-up;
- those that promote children's drug products by using nationally known persons or characters, e.g. cartoon characters, in the direct presentation of the product.

Preclearance of advertising

All drug advertisements presented in the electronic media — radio and television — must be precleared by the Drugs Directorate. This requirement originates with the Broadcasting Regulations administered by the Canadian Radio-Television and Telecommunications Commission.

Advertisements directed to the general public and appearing in the print media — newspapers, magazines, and direct mail pieces — are not subject to preclearance. They are, however, monitored on a continuing basis and are subject to the same type of legislative controls as are commercials used for broadcast. At the discretion of the manufacturer, the Directorate's opinion may be sought on print advertising material before it is used.

Advertisements directed to health professions in Canadian journals and direct mail pieces are subject to preclearance by the Pharmaceutical Advertising Advisory Board (P.A.A.B.), a non-governmental Board with representation from various professional and manufacturer's associations. The Health Protection Branch is consulted in an advisory capacity. Although the Branch is in agreement with the objectives of this outside Board, the Branch maintains the right under law to disagree with material directed to the health professions in Canada and to take appropriate action.

Packaging

Package requirements are derived in response to the various chemical and physical characteristics of the products they contain. Packages are designed to maintain the potency and purity of a drug for as long as possible. The package itself must not interact with the drug chemically.

Some examples of specialized drug packaging:

- A light-resistant container is needed for phenothiazine tranquilizers because light will diminish their potency and shelf life.
- A glass container is needed for nitroglycerin tablets, as the potency of these tablets will diminish if stored in a plastic container, which is semi-porous.

Bibliography

Food and Drug Regulations, with Amendments to October 1979 (Sections C.01.003 — C.01.005).

Health and Welfare Canada. 1974. *HPB Guide for Drug Advertisers* (available from HPB, Bureau of Drug Surveillance).

Prepared by and available from Educational Services:
Warning Labels on Headache Preparations — *Dispatch* No. 5

Truth in Drug Advertising — *Dispatch* No. 25

Chapter 7
The Drug Manufacturer

Drug manufacturing calls for meticulous care in all phases of its operation; the responsibility for quality control rests solely with the manufacturer. The government provides legislation and guidelines that establish minimum standard conditions under which drugs should be manufactured, processed, distributed, stored, tested, and packaged. Controls vary depending on the type of product, e.g. topical preparations require fewer controls than vaccines.

Premises and Equipment

- All surfaces must be easily cleaned.
- All processing, testing, finishing, distribution, and storage areas must be clean, sanitary, orderly, and free from waste and debris.
- Only materials and equipment required for the specific operation in progress should be present.
- The physical set-up of operations should be such that one drug does not contaminate another (cross-contamination).
- The equipment must be completely and thoroughly cleaned after each operation to prevent cross-contamination.

Qualifications of Personnel

People in charge of manufacturing and quality control must be trained professionals with a background in such sciences as chemistry, biochemistry, and pharmacology.

Raw Materials

These are substances used for the manufacture of a drug product. Each lot of raw material received in the plant must be tested for identity, purity, and potency. Material must be retested if held in storage for more than two years or more frequently if subject to rapid chemical or physical changes.

Storage

Drugs must be stored under conditions that maintain their potency, e.g. some drugs must be refrigerated.

Master Formula

This is a set of instructions stating in detail the materials, procedures, and precautions required to process and uniformly reproduce a specified quantity of drug product.

Product Testing

A finished product must be tested to ensure it meets its specifications (e.g. identity, potency, purity).

Packaging Materials

Packaging materials (labels, caps, bottles, enclosures, seals, papers, boxes, etc.) must be tested and examined for their suitability for the drug. Precautions must be taken to avoid mislabelling. Strict accounting is required for each label used, including rejects.

Monitoring

- Procedures should be double checked and work orders initialled.
- Accuracy and care should be exercised in weighing, measuring,

and mixing components into a batch.

- A product should be easily identified throughout the manufacturing process.

Sample Retention

Samples of each lot of finished drug must be kept for five years if the drug has no expiration date, and for one year beyond the expiration date if the drug has one. Samples of each lot of raw materials must be kept for two years from the date of their last use.

Record Keeping

A record must be maintained of all information pertinent to a drug product — information on raw material and finished product testing, packaging-material checks, adverse drug reactions, recalls or complaints received, lot and order numbers, and date of distribution of each product from the plant.

Recall System

A manufacturer selling a drug must maintain a system that permits rapid recall of any lot of drug.

Bibliography

Canadian Government Specifications Board Standard 74-GP-1e. Revised 1975. (Available from Department of Supply and Services.)

Food and Drug Regulations, with Amendments to October 1979. (Manufacturing Facilities and Controls, C.01.051 — C.01.056).

Health and Welfare Canada 1974. HPB *Guide for Drug Manufacturers*. (Available from HPB, Bureau of Drug Surveillance.)

Chapter 8
Monitoring Drug Safety and Quality

The Drug Identification Number (DIN/GP)

To facilitate its monitoring programs the Branch must be able to quickly identify all marketed drugs. Before a drug can be sold, a manufacturer must apply for and obtain a *drug identification number*, which must appear on the product label. Based on the data provided, the Branch maintains files which include the following information about every product on the market:

- names and addresses of persons or firms that appear on the label;
- name of the drug;
- use or purpose for which the drug is recommended;
- quantitative list of medicinal ingredients, i.e. active ingredients;
- copies of all labelling;
- pharmaceutical form, i.e. capsule, powder, liquid, etc.;
- recommended dosage;
- recommended route of administration;
- quantitative list of colouring agents.

Five characteristics are used to generate the six-digit identification number: the manufacturer, active ingredient, concentrations of active ingredients, route(s) of administration, and pharmaceutical form. This number provides the Branch with an inventory of all drugs on the Canadian market. It is prefixed by "GP" in the case of proprietary medicines and "DIN" for all other drugs.

If a manufacturer has two or more products identical in the five characteristics but differing in brand name or in non-medicinal ingredients (e.g. colour), the products would have the same DIN. There are more than 15 000 drug products on record as being sold in Canada.

Who uses the DIN/GP?

- Health Protection Branch,
- provincial governments,
- health insurance companies,
- professional associations,
- poison control information and treatment centres,
- hospitals and universities,
- drug manufacturers.

The Branch relies on the information in applications for DIN/GP for planning and scheduling, and in emergency situations requiring rapid identification of the product.

The Inspection

Under the Food and Drugs Act an inspector from HPB's Field Operations Directorate has the authority to enter and inspect a place where drugs are manufactured or stored. His task is to monitor compliance with the Act and Regulations, and he may also offer advice and guidance in interpretation of the legislation. The inspector is a trained professional, with qualifications similar to those of persons in charge of quality control in the plant (Chapter 7).

When inspecting a plant, the inspector observes production procedures in a logical sequence from receipt of components into the plant until the product is in a form ready for distribution; the inspection covers the premises and equipment, sanitation, personnel, quality control, records and samples, product information records, the recall system, and where relevant, special requirements for parenteral

drug production. Samples of products may be taken for subsequent examination.

At the end of the inspection, which may take several days, the inspector meets with the manufacturer to discuss the findings and indicates any changes requiring immediate attention. Serious deficiencies may result in prosecution and/or seizure of products.

Imported Drugs

About 18% of the drug products sold in Canada are imported. An importer must maintain comprehensive information to show that the imported drugs are manufactured to specifications and under conditions that meet Canadian requirements. In addition, the following are required:

- The name and address of the drug importer must appear on the label (except for Schedules C and D drugs, where this must appear on the licence).
- Records must be maintained of the drug distribution in Canada.
- Premises that manufacture Schedules C and D drugs (e.g. insulin, sera, vaccines, radiopharmaceuticals) must be inspected by Health Protection Branch inspectors and licensed before the drug can be imported.

To monitor the technical and scientific competence of foreign pharmaceutical firms and to provide for prompt communication on potential hazards, the Health Protection Branch exchanges information with agencies in other countries, e.g. U.S. Food and Drug Administration.

Analytical Programs

Each regional office of the Branch is equipped with a drug laboratory. Thousands of drugs are tested annually in these laboratories, which have fully qualified staffs comprising chemists, pharmaceutical chemists, microbiologists, and technologists, who are capable of determining such things as a drug's identity, potency, purity, sterility, dissolution rate, and disintegration time.

A specialized facility for national monitoring is located in the Ontario regional laboratory. This unit, the Drug Quality Monitoring Laboratory, is equipped for the automated determination of potency and content uniformity.

What drugs are analyzed?

- Drugs obtained as part of ongoing national monitoring surveys that help to assess the quality of drug products on the Canadian market.
- Drugs (usually controlled, narcotic, or restricted drugs) obtained from illicit channels and submitted by law enforcement agencies for identification (Drug Identification Service).
- Drugs whose quality is questioned by external sources e.g. general public, professional groups.
- Drugs obtained during an inspection, to ensure their compliance with the Act and Regulations.

Drug Quality Assessment Program (QUAD)

The QUAD program was initiated in 1971 to provide pharmacists, physicians, dentists, and other health professionals and purchasing agencies with information about the quality of drugs on the Canadian market. This information is based on the inspection reports and the analyses performed in the regional laboratories. At its inception nearly 400 products, representing 27 drug substances manufactured by 41 firms, were evaluated. Now the program has expanded to include more than 2000 products, representing over 235 substances manufactured by about 182 firms.

Complaints and Investigations

Investigations are conducted in response to complaints received from various sources outside the Branch. The primary sources of these complaints are consumers and health professionals. The investigation of these complaints begins by focusing attention on how the product has been used and handled by the individual or institution raising the concern. This is to determine whether the complaint has resulted from user, rather than manufacturer, error. When user error has been eliminated as a possible cause, the investigation proceeds to the level of the manufacturer and, where indicated, samples of the drug are analyzed in the Branch's laboratories.

Product complaints should be directed to the nearest regional or district office of the Health Protection Branch.

Drug Adverse Reaction Program

The Canadian Drug Adverse Reaction Program was initiated in 1965

- to assist the Branch (then called the Food and Drug Directorate) in monitoring drugs in use with a view to early detection of adverse drug effects;
- to advise the Branch on drug labelling and advertising with respect to warnings, contraindications, precautions, and adverse effects;
- to inform practitioners of the types and, where possible, the incidence of adverse reactions to drugs singly and in combination;
- to contribute information to the Adverse Reaction Program of the World Health Organization.

The Branch has developed a simple reporting form (Appendix II), familiar to most physicians, which is available on request to the health professions. All reports are handled in strictest confidence. More than 3000 reports are submitted annually by physicians, nurses, pharmacists, and drug manufacturers.

When a potential problem is identified, the manufacturer(s) is advised. If warranted, the drug may be withdrawn from the market. However, usually only minor changes are required, e.g. a change in prescribing information. Health professionals may be informed of the change by the manufacturer in promotional material or by the Branch in a letter.

Poison Control Program

When this program began in 1957, poison control centres were located in pediatric hospitals because most poisoning cases at that time involved children. Since then, however, the character of the poisoning problem has shifted. The number of adults and adolescents being poisoned has increased. The types of drugs and drug combinations have changed, with more adult poisoning deaths attributed to the use of multiple products (taking excessive amounts of more than one type of drug) and more poisonings with tranquilizers among persons five years of age and older. Also, while the number of accidental poisonings seems to be levelling off, the number of intentional poisonings is increasing.

Today there are more than 300 poison control centres coordinated in a national network. The centres are under the direction of the provincial departments of health, but the collection, coordination, and dissemination of information to the centres is handled by the Health Protection Branch.

Statistics on poisoning cases reported by the centres are computerized and appear annually in *Poison Control Program Statistics*, a Branch publication. The statistics indicate which products need to be more carefully controlled through measures such as ingredient changes, child-resistant packaging, and improvements in labels and warnings.

Ingredient information on over 12 000 products has been entered into a card catalogue system along with treatment advice and has been distributed by the Branch to poison control centres across the country. This enables the centres to respond to enquiries on product ingredients.

The Branch has also published a booklet, *Poisons — Emergency Treatment*, in cooperation with the Canadian Paediatric Society. This publication is available to poison control centres and health professionals.

Most telephone directories list an emergency poison control centre number where health professionals and the general public can report a poisoning and obtain immediate advice on what measures to take.

Bibliography

Health and Welfare Canada:

— Published Annually. *Canadian Drug Identification Code* (available from HPB, Bureau of Drug Surveillance).

— 1971. Drug Adverse Reaction Reporting Program. *Rx Bulletin* 2(9): 139-141.

— 1971. FDD's Poison Control Program — A seven-year review. *RX Bulletin* 2(8): 121-128.

— 1971. *Guide for Preparation of Plant Master Files and Imported Drug Submissions* (available from HPB, Bureau of Drug Quality Assessment).

— 1973. Poisoning in Canada. *Rx Bulletin* 4(8): 184-185.

— 1975. *Poison Control Program Statistics* (available from HPB, LCDC, Bureau of Epidemiology).

— 1977. *Poisons — Emergency Treatment*. Prepared by the Safety Promotion Committee of the Canadian Paediatric Society (available from HPB, LCDC, Bureau of Epidemiology.)

Prepared by and available from
Educational Services:

— A Day in the Life of a Drug Inspector
Dispatch No. 18

— A Cause for Complaint — *Dispatch*
No. 34

— *Think About It* (prevention of accidental poisoning) — leaflet

— *Handle With Care* (steps to take if a poisoning occurs) — leaflet

Chapter 9
Enforcement/Compliance

Most drug manufacturers and distributors comply with legislation. Thus, the Branch's basic philosophy is one of "voluntary compliance." As a result, when a violation is uncovered, and the matter is not serious, the manufacturer or distributor may be given the opportunity to correct the defect, but under the watchful eye of the Branch's field inspectors. This is often the only action required.

However, when, in the judgment of the Branch, a given situation is a serious one, or after repeated less serious matters have come to the attention of the Branch, it may and does initiate prosecution procedures.

Seizure

An inspector has the power to seize products in violation or suspected to be in violation of legislation. A seizure may be made at the manufacturing, distributing, or retail level and may occur for various reasons, e.g. labelling infractions, unsanitary storage conditions, failure of the drug to meet its standard.

If seized products are found to be in compliance on further analyses or if the manufacturer rectifies the problem, the drugs are released for sale. If the products are not in compliance and the problem is not one that can be corrected by the manufacturer, then the products are destroyed or otherwise disposed of as the Minister directs.

Refused Entry

Imported drugs may be detained or refused entry at the time of importation. If the product defect cannot be corrected, the drugs are denied entry; if the defect can be corrected the importer may be permitted to receive the shipment on condition that correction be made within a specified time.

Recalls

Drug manufacturers receive information concerning product defects from a variety of sources, including the Health Protection Branch. As a result, the manufacturer may initiate a recall of the product. Detailed information relating to the defect and the extent of the recall (distributor or retail level) must be supplied to the Branch. The Branch will use this information and/or information from its monitoring sources in deciding whether the product defect represents a serious health hazard. If there is a threat to the safety of the consumer, a public alert will be issued through the news media.

In cooperation with the provincial and municipal health agencies and with industry associations, the Branch has established a National Emergency Recall Plan to deal with widespread health hazards at the general public level. For example, if a commonly used OTC were contaminated with strychnine, the Plan would enable the Branch to mobilize many people at different levels of government (federal, provincial, and municipal) to correct the problem. A public alert would also be issued. In practice, the Plan has never been implemented in the recall of a drug. Recalls of drugs in the past have not necessitated such mobilization of manpower.

Protection

The Field Operations Directorate publishes *Protection*, a quarterly report of enforcement actions taken by the Branch. *Protection* is sent to all manufacturers, provincial departments of health, the media, educators, health professionals, and to associations dealing with groups such as consumers and importers.

Bibliography

Health and Welfare Canada, Health Protection Branch. *Protection*. Quarterly compliance report. (Available from HPB, Bureau of Field Operations.)

Chapter 10
Biologics, Radiopharmaceuticals, Sensitivity Discs

Biologics

These drugs are listed in Schedules C and D to the Food and Drugs Act. Biologics are made from living organisms and their products or are synthesized. Examples of biologics are insulin and anterior pituitary extracts (Schedule C) and sera, vaccines, and parenteral antibiotics (Schedule D).

Because the manufacturing of these drugs is so intricate and so critical to the final product (e.g. diminishing the virulence of the polio virus to produce a vaccine), the premises in which they are manufactured must be inspected and licensed before the drug can be sold in Canada. This also applies to biologics manufactured in foreign countries for sale in Canada. The Bureau of Biologics, Drugs Directorate, carries out the inspection and issues the licence. The Bureau has its own laboratories for routinely testing these drugs for safety and efficacy.

Note that a drug listed in Schedules C or D may also be listed in Schedule F to the Regulations. The first two schedules regulate how the drug is manufactured; the latter schedule states under what conditions it can be made available to the general public (i.e. via prescription).

Radiopharmaceuticals

These drugs, listed in Schedule C to the Act, emit alpha, beta, or electromagnetic radiations and are used primarily for diagnostic procedures and cancer therapy. Because of their radioactive emissions, careful and exact controls must be implemented in their manufacture and distribution. Thus the same requirements for licensing other Schedule C drugs (above) apply to radiopharmaceuticals.

Plants where radiopharmaceuticals are produced are inspected by both the Bureau of Biologics, Drugs Directorate, and the Radiation Protection Bureau, Environmental Health Directorate. The Radiation Protection Bureau also acts as principal health and medical advisor to the Atomic Energy Board of Canada, the agency that controls the use of radioactive materials, including radiopharmaceuticals.

Sensitivity Discs and Tablets

These are absorbent materials or tablets (Schedule E to the Act) impregnated with one or more antibiotics, sulphonamides, or other preparations that possess inhibitory action on the growth of microorganisms. They are used as a diagnostic aid in determining the sensitivity of a disease-causing agent to the drug which the disc or tablet contains.

Because of the low level of drugs in these products and the importance of results in establishing a course of treatment, samples of each lot are tested in the laboratory of the Bureau of Biologics before they can be released for sale in Canada.

Bibliography

Health and Welfare Canada. 1974. Radiopharmaceuticals. *Rx Bulletin* 5(3): 47-48

Chapter 11
Controlled, Narcotic, and Restricted Drugs

Drugs listed in Schedule G (controlled) and Schedule H (restricted) to the Food and Drugs Act and those listed in the Schedule to the Narcotic Control Act (narcotic) may have habit-forming properties and are subject to abuse. Consequently it is an offence to possess any of these drugs for the purpose of trafficking. For restricted and narcotic drugs it is also an offence to possess them for reasons other than those covered by the Food and Drugs Act and Regulations and the Narcotic Control Act and Regulations. To prevent the flow of these drugs from legal to illegal sources, additional controls are imposed on their manufacture, distribution, and sale.

Licensed Dealer

Only dealers licensed by the Department may manufacture, import, or export these drugs; the licensed dealer must maintain detailed records of all transactions for a minimum of two years.

Record Keeping

Records must account for

- all drugs received, their source, date received;
- all drugs supplied, to whom, date shipped;
- all drugs manufactured, quantity produced, date;
- monthly inventory of all stock on hand.

Pharmacists and physicians must also maintain similar detailed records on all their transactions with controlled and narcotic drugs.

Auditing the Records

Inspectors from the Bureau of Dangerous Drugs, Drugs Directorate, audit the records of licensed dealers, pharmacists, practitioners, and hospitals.

Sale of Narcotic and Controlled Drugs by the Licensed Dealer

With the exception of methadone (used in the treatment of heroin addiction), a licensed dealer may sell these drugs only to another licensed dealer, pharmacist, practitioner, hospital, Regional Director of the Health Protection Branch, or a person authorized by the Minister of the Department of National Health and Welfare to be in possession of such drugs.

Import and Export Controls

For each shipment of these drugs imported into and exported from Canada, a licensed dealer requires a permit that states the source and destination of the shipment and the port of entry or exit.

Single Convention on Narcotic Drugs

The Bureau of Dangerous Drugs maintains a liaison and cooperates with international drug enforcement agencies and foreign government units in areas of mutual interest. It provides quarterly and annual reports and statistics to the International Narcotic Control Board, as required under the 1961 Single Convention on Narcotic Drugs (United Nations).

Chapter 12
Educational Services

All programs of the Health Protection Branch are ultimately directed towards ensuring that the products for which it is responsible are safe and effective when used by the consumer.

To aid the Branch in informing Canadians about the food and drug laws and Branch activities, a specialized professional group (the Educational Services Consultants) is attached to the five regional and two district offices of the Branch. They work with the media and with other regional groups such as teachers, community workers, consumer associations, provincial government departments, and professional societies.

The coordinating office of Educational Services is in Ottawa. Here the broad goals of the program are established and resource materials such as booklets, fact sheets, audio visual aids, and bulletins are generated.

An Educational Services consultant may be contacted at the following addresses:

Health Protection Branch,
Room 618, Customs Building,
1001 West Pender Street,
VANCOUVER, B.C.
V6E 2M7

Health Protection Branch,
Room 30, Commonwealth Building,
9912-106 Street,
EDMONTON, Alberta
T5K 1C5

Health Protection Branch,
310 Federal Building,

269 Main Street
WINNIPEG, Manitoba
R3C 1B2

Health Protection Branch,
2301 Midland Avenue,
SCARBOROUGH, Ontario
M1F 4R7

Health Protection Branch,
1001 St. Laurent West,
LONGUEUIL, Québec
J4K 1C7

Health Protection Branch,
Box 6396,
Station "A",
SAINT JOHN, New Brunswick.
E2L 4L9

Health Protection Branch,
Ralston Building,
1557 Hollis Street,
HALIFAX, N.S.
B3J 1V5

Appendix I

Schedule A

No person shall advertise any food, drug, cosmetic or device to the general public as a treatment, preventative or cure for any of the diseases, disorders or abnormal physical states mentioned in Schedule A.
(Subsection 3(1) Food and Drugs Act)

Schedule A, reproduced below, was enacted to prevent advertising claims directed to the general public for serious diseases, disorders, or abnormal physical states, which can only be diagnosed and treated by a medical practitioner, and for diseases with no known cures:

Alcoholism
Alopecia
Anxiety state
Appendicitis
Arteriosclerosis
Arthritis
Bladder disease
Cancer
Convulsions
Depression
Diabetes
Disease of the prostate
Disorder of menstrual flow
Dysentery
Edematous state
Epilepsy
Gall bladder disease
Gangrene
Glaucoma
Gout
Heart disease
Hernia
Hypertension
Hypotension
Impetigo
Influenza
Kidney disease
Leukemia
Liver disease
Nausea and vomiting of pregnancy
Obesity
Pleurisy
Pneumonia
Poliomyelitis
Rheumatic fever
Scabies
Septicemia
Sexual impotence
Tetanus
Thyroid disease
Tuberculosis
Tumor
Ulcer of the gastro-intestinal tract
Vaginitis
Venereal disease

Appendix II

Health and Welfare Canada — Santé et Bien-être social Canada
Health Protection Branch — Direction générale de la protection de la santé

REPORT OF AN ADVERSE REACTION OR EVENT SUSPECTED DUE TO DRUGS, VACCINES*, COSMETICS OR FOOD PRODUCTS

In confidence to: Poison Control and Adverse Reaction Programs Division

PATIENT DATA

PATIENT IDENTIFICATION | AGE | SEX ☐ MALE ☐ FEMALE | WEIGHT | HEIGHT

CHART NUMBER | ETHNIC ORIGIN | ALLERGIES OR PREVIOUS ADVERSE REACTIONS ☐ YES (*Specify*) ☐ NO

CONDITIONS PRIOR TO REACTION

ADVERSE REACTION OR EVENT

REACTION ONSET WAS ☐ GRADUAL ☐ SUDDEN Specify in min / hrs ☐ OTHER (*Specify*)

DESCRIPTION OF THE ADVERSE REACTION OR EVENT | ONSET OF REACTION Day Month Year | LABORATORY VALUES

INTENSITY OF REACTION OR EVENT ☐ MINOR ☐ MODERATE ☐ MAJOR ☐ HOSPITALIZED ☐ NOT HOSPITALIZED

TREATMENT OF REACTION

— SUSPECTED DRUG WAS ☐ STOPPED ☐ DOSE REDUCED ☐ UNCHANGED ☐ OTHER (*Specify*)

— TREATMENT DRUGS OR THERAPY ☐ YES (*Specify*) ☐ NO

OUTCOME OF REACTION ☐ RECOVERED ☐ RECOVERED WITH RESIDUAL EFFECTS ☐ NOT YET RECOVERED ☐ UNKNOWN ☐ FATAL Date and cause

PRODUCT DATA

SUSPECTED DRUGS OR PRODUCTS Trade name / Chemicals / Batch & Lot No	DATES STARTED	DATES ENDED	DRUG DATA DAILY DOSE	DRUG DATA ROUTE	REASON FOR USE

DRUGS TAKEN CONCOMITANTLY ☐ YES (*Specify*) ☐ NO

OTHER COMMENTS

HOSPITAL'S NAME | COMPLETED BY | H P B USE ONLY

CITY | PROVINCE

HPB 5069 (9-78) *Use reverse side if necessary* *Français au verso*

Glossary

Addictive — any substance that tends to induce a physiological or psychological dependency

Adulterate — to corrupt, debase, or make impure by the addition of a foreign or inferior substance

Amphetamines — a group of drugs used as stimulants of the central nervous sytem

Antibiotic — a drug that suppresses the growth of microorganisms in the body and helps control diseases of infectious origin

A.S.A. — acetylsalicylic acid

Assay — laboratory analysis to determine the presence, absence, or quantity of one or more substances

Barbiturates — a group of drugs used as sedatives or sleep-inducing agents

B.P. — the British Pharmacopoeia — a series of drug standards

B.P.C. — the British Pharmaceutical Codex — a series of drug standards

C.F. — the Canadian Formulary — a series of drug standards

C.S.D. — Canadian Standard Drugs — a Food and Drugs Act standard assigned to a specific group of drugs

Canada Gazette — a government publication listing all new legislation becoming effective at any given time

Cosmetic — any substance or mixture of substances manufactured, sold, or represented for use in cleansing, altering, or improving the complexion, skin, hair, or teeth, includes deodorants and perfumes

DIN — drug identification number — a six digit, computer-generated number assigned to a specific drug product

Designated Drugs a group of amphetamine-type stimulant drugs subject to abuse that can only be used in the treatment of designated diseases in humans and animals

Drug a drug is a substance manufactured or sold or represented for use in (a) the diagnosis, treatment, mitigation, or prevention of a disease, disorder, abnormal physical state, or the symptoms thereof, in man or animal; (b) restoring, correcting, or modifying organic functions in man or animal; or (c) disinfection in premises in which food is manufactured, prepared, or kept, or for the control of vermin in such premises

Enteric a drug specifically coated to pass through the stomach unaltered and disintegrate in the upper intestines

Epidemiology a science dealing with the incidence, distribution, and control of disease in a population

Epilepsy a disorder marked by disturbed electrical rhythms of the central nervous system typically manifested by convulsions and clouding of consciousness

Excipient non-active ingredient in a drug compound

GP letters preceeding a number assigned to a drug for purposes of identification and registration as a proprietary medicine

Hyperkinetic abnormally increased and usually purposeless and uncontrollable muscular movement

IU International Units — a quantity of a biological (as in a vitamin) that produces a particular biological effect — agreed upon as an international standard

Identity the chemical composition constituting a drug in its given form

LSD lysergic acid diethylamide — a hallucinogenic drug subject to abuse and therefore available only to institutions involved in highly specialized research due to high abuse

Label any legend, word, or mark attached to or accompanying a drug or package; an "inner label" is the label on the container; "outer label" is on the package of a drug

Lot number any combination of letters, figures, or both by which any drug can be traced in manufacture and identified in distribution.

N.F. the National Formulary — a series of drug standards

Narcolepsy a condition characterized by brief attacks of sleep

Narcotic a drug that in moderate doses dulls the senses, relieves pain, and induces profound sleep, but has a high potential for addiction leading to abuse

OTC Over-the-counter (non-prescription) preparation for self-medication

Ophthalmic of or relating to the eye

Package includes anything in which any food, drug, cosmetic, or device is wholly or partly contained, packed, or placed

Parenteral a drug that is not introduced to the body by means of absorption through the intestinal wall, but by syringe or other instrument

Pathophysiology the physiology of abnormal states; the functional changes that accompany a particular disease or syndrome

pH symbol commonly used to measure or indicate the acidity or alkalinity of a solution

Pharmacodynamics a branch of pharmacology dealing with the reactions between drugs and living structures

Pharmacokinetics the study of the bodily absorption, distribution, metabolism, and excretion of drugs

Ph.F. Pharmacopée Française — a set of drug standards

Ph.I. Pharmacopoeia Internationalis — a set of drug standards

Potency a measure of the chemical or medicinal effectiveness of a substance

Prescription an order given by a practitioner, directing that a stated amount of a drug or mixture of drugs specified therein be dispensed for the person named in that order

Proprietary or Patent Medicine Act (PPM) act of legislation by the Canadian government in 1909 in response to a public concern over patent medicines. Repealed in 1977

Psychotropic a compound that has the ability to modify mental activity

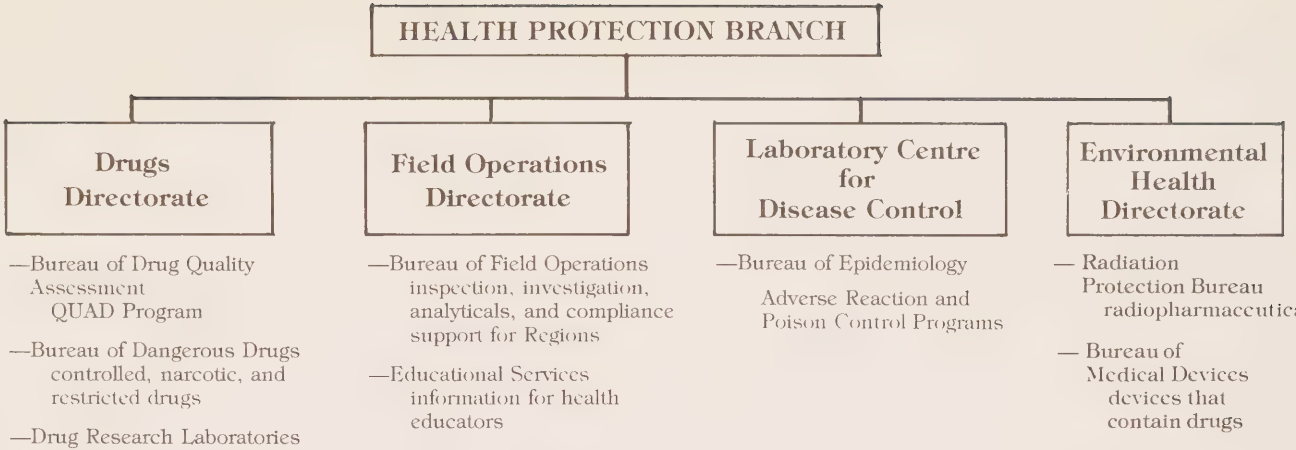
Purity the absence of foreign substances in a specific drug

Pyrogen a fever-producing substance

Residue a remainder; that which remains after the removal of other substances

Standard a criterion set up and established by authority as a rule for the measure of quality, weight, value, or quantity

Synthetic chemical compound built up in a laboratory by the fusing of its various elements; possesses the same molecular structure as its corresponding naturally occurring compound, when there is a naturally occurring compound



2/80

Chart reflecting the drug organization of the Health Protection Branch, Health and Welfare Canada, Tunney's Pasture, Ottawa K1A 1B7

FUTURE REVISION OF HEALTH PROTECTION AND DRUG LAWS DEPENDS ON YOU

Please answer the following questions and return form to:
Educational Services, Health Protection Branch, Health and Welfare Canada, Ottawa, Canada K1A 1B7

1. OCCUPATION:

Health professional ☐ 1 Educator ☐ 2 Drug industry personnel ☐ 3

Other (please specify) ☐ 4 _____

Student: pharmacy ☐ 5 law ☐ 6 other (please specify) ☐ 7 _____

2. HOW DID YOU FIND OUT ABOUT THE PUBLICATION?

Advertisement ☐ 1 Flyer ☐ 2 Word of mouth ☐ 3

Other (please specify) ☐ 4 _____

3. DID YOU FIND Satisfactory(S)/Unsatisfactory(U)

References ☐ 1
Format ☐ 2
Content ☐ 3

COMMENTS: _____

_____

4. HOW DO YOU USE THIS PUBLICATION?

Personal reference ☐ 1 Educational material ☐ 2

Other (please specify) ☐ 3 _____

5. HAVE YOU RECOMMENDED THIS PUBLICATION TO

Health professional ☐ 1 Educator ☐ 2 Drug industry personnel ☐ 3

Student ☐ 4 None ☐ 5 Other ☐ 6 _____

6. ANY SPECIFIC COMMENTS OR SUGGESTIONS FOR REVISIONS?

_____

_____

Health Protection and Drug Laws

Health and Welfare Canada
Santé et Bien-être social Canada

Canada

Government Publications

Health Protection and Drug Laws

Educational Services
Health Protection Branch
Department of National Health and Welfare

Published by authority of the
Minister of National Health and Welfare
10/82

Également disponible en français sous le titre
"Les médicaments, la santé et la loi"

Available in Canada through

Authorized Bookstore Agents
and other bookstores

or by mail from

Canadian Government Publishing Centre
Supply and Services Canada
Ottawa, Canada, K1A 0S9

Catalogue No. H 49-5/1983E
ISBN 0-660-11232-9

Canada: $2.95
Other countries: $3.55

Price subject to change without notice

Evaluation
Health Protection and Drug Laws

Future Revision of "Health Protection and Drug Laws" Depends on You

Please answer the following questions and return form to: Educational Services, Health Protection Branch, Health and Welfare Canada, Ottawa, Canada K1A 1B7

1. OCCUPATION

Administration	☐ 1	Paramedical	☐ 6	Student/Pharmacy	☐ 10
Education	☐ 2	Pharmacist	☐ 7	Student/Law	☐ 11
Inspection	☐ 3	Drug Industry		Other	☐ 12
Med/Dentistry	☐ 4	Personnel	☐ 8	(please specify)	
Nursing	☐ 5	Other Health Professional	☐ 9		

2. HOW DO YOU USE THIS PUBLICATION?

Personal Reference	☐ 1	
Educational Tool	☐ 2	(Please specify)_____
Other	☐ 3	(Please specify)_____

3. HOW WOULD YOU RATE THE VARIOUS SECTIONS OF THIS BOOK?

Section	Very Useful	Useful	Needs Improvement	Unsatisfactory	Did Not Use
1. Perspective	1	2	3	4	5
2. Drugs and their Availability	1	2	3	4	5
3. Record Keeping and the Prescription	1	2	3	4	5
4. New Drugs	1	2	3	4	5
5. Drug Standards	1	2	3	4	5
6. Advertising/Labelling/ Packaging	1	2	3	4	5
7. The Drug Manufacturer	1	2	3	4	5
8. Monitoring Drug Safety and Quality	1	2	3	4	5
9. Enforcement/ Compliance	1	2	3	4	5
10. Biologics, Radio-pharmaceuticals	1	2	3	4	5
11. Controlled, Narcotic and Restricted Drugs	1	2	3	4	5
12. Glossary	1	2	3	4	5

If you suggest improvement is needed, please identify, on a separate page, the sections and indicate the improvement needed (e.g. organization, depth, completeness) _____

4. HOW WOULD YOU RATE THE FOLLOWING ASPECTS OF THE BOOK?

	Satisfactory	Unsatisfactory
Organization	1	2
Amount of Information	1	2
Depth of Information	1	2
Level of Language	1	2

Comments _____

5. HAVE YOU RECOMMENDED THIS PUBLICATION TO?

Health professional ☐ 1 Educator ☐ 2 Drug industry personnel ☐ 3
Student ☐ 4 No one ☐ 5 Other ☐ 6

6. WHAT OTHER INFORMATION OR SUBJECT AREAS WOULD YOU LIKE TO SEE INCLUDED IN FUTURE EDITIONS? _____

7. HAVE YOU ANY SPECIFIC COMMENTS OR SUGGESTIONS FOR REVISIONS?

Thank you for taking the time to help us improve "Health Protection and Drug Laws."

Contents

Introduction

Two acts form the basis of the drug laws: the *Food and Drugs Act* and the *Narcotic Control Act*. The responsibility for administering these acts rests mainly with the Health Protection Branch, Department of National Health and Welfare (see the chart reflecting the various drug responsibilities of the Branch.)

Why have drug laws? What are the drug laws? How are these laws implemented? It is the purpose of this publication to answer these three questions. The answers are directed mainly at health professionals, students in the health professions, consumer advocate groups, and students of consumer protection laws. It is hoped that this publication will be useful in their dealings with the general public, the government, and industry.

Because the volume of legislation that can be outlined in this type of publication is limited, the reader who wants more detail may use this guide in conjunction with the Acts and Regulations and may also refer to the source material listed in the bibliography at the end of each chapter.

A glossary of terms is included at the end of the booklet.

HEALTH PROTECTION BRANCH

Drugs Directorate

—Bureau of Drug Quality
QUAD Program

—Bureau of Dangerous Drugs
controlled, narcotic, and restricted drugs

—Bureau of Drug Research
drug research programs

—Bureau of Human Prescription Drugs
new drug submissions (drugs for human use)

—Bureau of Veterinary Drugs
new drug submissions (drugs for veterinary use)

—Bureau of Nonprescription Drugs
evaluation of marketed drugs (advertising, labelling, and DIN)

—Bureau of Biologics
inspection, new drug submissions, analysis and licensing of Schedule D drugs (biologics)

Field Operations Directorate

—Bureau of Field Operations
inspection, investigation, analysis, and compliance support for Regions

—Educational Services
information for health educators and consumers

Regional Offices located in
Vancouver, B.C.
Winnipeg, Man.
Toronto, Ont.
Montreal, Que.
Halifax, N.S.

and 22 District Offices

Laboratory Centre for Disease Control

—Bureau of Epidemiology
Adverse Reaction and Poison Control Programs

Environmental Health Directorate

—Radiation Protection Bureau
radiopharmaceuticals

—Bureau of Medical Devices
marketing control and evaluation of medical devices, including those containing drugs

10/82

Chart reflecting the drug organization of the Health Protection Branch, Health and Welfare Canada, Tunney's Pasture, Ottawa K1A 0L2

Chapter 1
Perspective

Evolution of the Drug Laws

Laws are a means of ensuring that drugs are safe and effective and are being used wisely. The acts that detail these laws, the *Food and Drugs Act* and the *Narcotic Control Act*, evolved from different pieces of legislation.

Food and Drugs Act

Inland Revenue Act (1875)
Dealt mostly with the adulteration of alcohol; drugs not defined. Forerunner of more effective legislation.

Adulteration Act (1884)
Defined drug, adulteration and conditions under which adulteration might take place.

Repealed

Food and Drugs Act (1920)

Food and Drugs Act (1953)
Controls manufacture, distribution, and sale of drugs except narcotics. Drugs formerly listed under PPM Act are now governed by this Act.

Proprietary or Patent Medicine Act (1909) Passed because of concern over efficacy and safety of secret-ingredient drugs.

Revoked
1977

Narcotic Control Act

Opium Act (1908)
Prohibited the unauthorized importation and possession of gum or smoking opium.

Opium and Drug Act (1911)
Included other problem drugs, e.g. cocaine and morphine.

Opium and Narcotic Control Act (1920)
Illicit trade in narcotics was increasing; more control necessary.

Narcotic Control Act (1961)
Controls the manufacture, distribution, and sale of narcotic drugs.

The Regulations

The Acts contain broad statements relating to safety and efficacy. The more detailed technical requirements are outlined in the Regulations.

The Regulations are also a means of rapidly updating legislation; they have the same force and effect as the Act itself.

Requests for changes arise from many sources: the government, professional or trade organizations, consumer groups, and industry. When identifying the need for new or changed regulations, the Branch considers such subjects as health hazards, fraud, surveillance problems, and international standards. Proposed changes are communicated to the drug industry, health professionals, and consumers by means of the *Information Letter*, distributed by the Health Protection Branch. Comments submitted by these concerned parties is considered in the drafting of new legislation.

The proposed regulation is reviewed by the Minister of National Health and Welfare, and if the Minister agrees, it is presented to the Governor-in-Council (a committee of the Cabinet) for passage. When passed, it is published in the *Canada Gazette*, Part II, which is issued twice monthly and contains all new and amended federal regulations.

Branch Communications

The Health Protection Branch (HPB) maintains constant contact with the drug industry and various professional and consumer groups. Such communications are vital for mutual understanding of roles and concerns and for obtaining the best possible advice in the development of new policies and regulations.

A continuing liaison is maintained with many professional organizations in such fields as pharmacy, medicine, dentistry, and veterinary medicine. Experts from these organizations are invited to sit on committees to advise the Branch on contentious or developing issues. For example, the Committee on Reproductive Physiology provides recommendations to the Branch relating to physical or chemical alterations of normal and abnormal reproductive physiology in males and females. The recommendations of the Committee have resulted in modifications of some products containing

estrogens, additional label warnings on others, a revision of the patient package insert for oral contraceptives, and the discontinuance of the sale of some oral contraceptives, including the sequentials.

The Branch also maintains contact with national organizations concerned with specific diseases (e.g. arthritis, cancer, diabetes) and consumer groups through its central office in Ottawa and its five regional offices across Canada.

Bibliography

Morrison, A.B. 1975. The Canadian approach to Food and Drug Regulations. *Food, Drug, Cosmetic Law Journal* 30: 632-643.

Pugsley, L. I. 1967. The administration and development of federal statutes of foods and drugs in Canada. *Medical Services Journal, Canada* 23 (3): 387-449.

Prepared by and available from Educational Services:

Protection is our Middle Name — *leaflet*

Canadian Drug Laws and the Consumer — *Dispatch* No. 33

The Canadian Food and Drugs Act and Regulations and the Narcotic Control Act and Regulations may be purchased from:

Supply and Services Canada
Canadian Government Publishing Centre
Ottawa, Canada K1A 0S9

Chapter 2
Drugs and their Availability

> *A drug is any substance used in the diagnosis, treatment, mitigation, or prevention of a disease, disorder, or abnormal physical state, and in restoring, correcting, or modifying organic functions, in man or animals.*
> (Paraphrased from the Food and Drugs Act)

Availability of drugs is governed by considerations of safety and effectiveness, i.e. the potential for misuse and the amount of professional consultation needed. At one end of the spectrum are drugs such as A.S.A. (acetylsalicylic acid) that may be bought in a grocery store by any person; at the other end are drugs such as LSD (lysergic acid diethylamide) that may be obtained legally only by a research institution with an authorization from the Minister of National Health and Welfare. The former can provide relief from a minor headache, easily self-diagnosed; the latter has no known medicinal use.

The health professional — physician, dentist, pharmacist, nurse, veterinarian — plays an important role in monitoring the availability of drugs to the general public. The amount of involvement depends on safety considerations. Federal laws provide many of the guidelines on availability, but provincial laws may further restrict the availability of a drug. The practice of pharmacy is regulated provincially.

Vaccines, Sera, Radiopharmaceuticals, Antitoxins

Drugs such as these are administered by a physician or a nurse, when required. The patient does not normally have access to these drugs, except through the physician.

Nonprescription Drugs

While it is not possible to completely categorize these drugs, generally speaking, they fall into three groups, and as their name suggests, they may be obtained without a medical prescription.

The Proprietary Medicines (or GPs as they are sometimes called) are those which may usually be purchased in any retail outlet. They may be identified by the label which shows a six-digit number preceded by the letters GP. Their use is intended for the symptomatic treatment of minor self-limiting illnesses which do not require the advice or intervention of a health professional. Examples of GPs are some minor pain relievers, medicated shampoos, cough drops, etc.

The second group also carries a six-digit number on the label, headed, however, by the letters DIN. For the most part, they are available only in pharmacies and are frequently referred to as OTCs (Over-the-counter drugs). They too are intended to relieve the symptoms of minor self-limiting illnesses, but for certain of these medicines it is recommended that the advice of a health professional be obtained concerning their use. Examples of these medicines include some laxatives, cough and cold remedies, sinus

and/or nasal preparations and many vitamins.

The third and smallest group are those which should be used only upon consultation with and recommendation by a physician. They are occasionally intended for long-term use. Medicines such as insulin, nitroglycerin, muscle relaxants and anti-spasmodics are examples of such medicines.

Drug or cosmetic?

Some products may be perceived by the general public to be cosmetics, but because they alter bodily functions are by definition drugs and are regulated as such (all are nonprescription drugs) e.g.:

- A toothpaste is a cosmetic when it cleans, whitens, and brightens the teeth; it is a drug when an ingredient, such as fluoride, is added to help prevent tooth decay.
- A deodorant is a cosmetic because it masks odor in perspiration; an antiperspirant is a drug because it suppresses the flow of perspiration.

Federal vs. provincial laws

Some drugs are nonprescription drugs federally but prescription drugs provincially. For example:

British Columbia	ephedrine and its salts (for internal use containing ephedrine as the single active ingredient)
Ontario	digitalis, its glycosides or derivatives

Prescription Drugs

Many drugs are available to the general public only after consultation with a practitioner (a physician, dentist or veterinarian) and the presentation of a prescription to a registered pharmacist. A prescription is an order given by a practitioner directing that a stated amount of a drug be dispensed for the person named in the order.

The main reasons for requiring additional control for these drugs are the need for professional direction and supervision in their use and in some cases their potential for abuse or misuse.

Types of prescription drugs are listed below; they are categorized according to the extent of control necessary for their safe use.

Vitamins A and D

Although usually sold as nonprescription drugs, preparations of vitamins A and D for humans require a prescription when the maximum daily dose recommended on the label exceeds 10 000 and 1000 IU, respectively. Large doses of such vitamins can be toxic.

Schedule F Drugs Pr

More than 200 drug substances are listed in Schedule F to the Food and Drug Regulations and represent a wide diversity of classes, such as antibiotics, hormones, and tranquilizers. Schedule F, perhaps more than any other, is subject to frequent changes. These result from the discovery and introduction to the marketplace of new drug substances, the identification of hazards of certain nonprescription

drugs, and knowledge of changing abuse and misuse patterns.

The symbol [Pr] must appear on labels of these drugs.

Controlled drugs ◇C

At present about 14 drugs are classified as controlled drugs and are listed in Schedule G to the Food and Drugs Act. They are stimulants (e.g. amphetamines, methamphetamines) and sedatives (e.g. barbituric acid, methaqualone).

The symbol ◇C must appear on labels and all professional advertisements.

One of the effects of amphetamines, methamphetamines, phendimetrazine, and phenmetrazine is the depression of appetite; thus these drugs became popular in the treatment of obesity. Because these drugs have a mood-modifying effect and can be habit-forming, they created more serious problems than the condition they were being used to treat. Hence, they are now also referred to as "Designated Drugs" and can only be prescribed for the following conditions:

Humans	narcolepsy, hyperkinetic disorders in children, mental retardation (minimal brain dysfunction), epilepsy, parkinsonism, hypotensive states associated with anesthesia
Animals	depression of cardiac and respiratory centres

Narcotic drugs "N"

Narcotic drugs are controlled by the Narcotic Control Act and Regulations and are listed in the Schedule to that Act. Examples of drugs in this group are cocaine, opium, codeine, morphine, phencyclidine, and cannabis (marihuana).

Some of these drugs have a legitimate medicinal use such as the relief of pain. However, their psychotropic effects (ability to modify mental activity) and addictive properties have led to stringent restrictions on their availability.

The letter "N" must appear on all labels and professional advertisements.

Codeine: the only narcotic preparations that can be sold to the general public without a prescription are oral preparations of codeine phosphate or its equivalent in concentrations not more than
8 mg/tablet or other solid form
20 mg/28mL
(Section 27, Narcotic Control Regulations).
Such products must also contain at least two additional medicinal ingredients (e.g. A.S.A., pheniramine maleate) in specified proportions.

Restricted Drugs

These substances, which have hallucinogenic properties (alter perception from objective reality with serious physiological and psychological effects), have no recognized medicinal use and are dangerous. There are about 23 such chemicals, which are listed in Schedule H to the Food and Drugs Act. The most well known is lysergic acid diethylamide (LSD). These chemicals are only available to institutions involved in highly spe-

cialized research. An authorization is required from the Minister of National Health and Welfare before such a drug can be sold.

Veterinary Drugs

Drugs listed in Part I of Schedule F to the Food and Drug Regulations may be sold only on prescription, whether for human or veterinary use. A prescription is not required for drugs listed in Part II, provided they are in a form that can only be used for animals or are labelled that they are for agricultural use only.

Drug residues in food

Such residues can have serious health consequences in terms of toxicity and allergic responses in sensitive individuals. To minimize this risk the labels of most veterinary drugs used in food-producing animals must specify the withdrawal period, i.e. the time between the last treatment of the drug and the use of the animal for food, either by slaughtering or the collection of milk or eggs. This period must elapse to ensure that residues of the drugs have been eliminated from any edible products derived from the animal.

Any antibiotic that leaves traces in the milk of lactating cattle longer than 96 hours after administration must not be used for their treatment. Also, different antibiotics are found in Parts I and II of Schedule F. Those found in Part I are more likely to persist in food and therefore require the additional control of a prescription when being used for animals.

Medicated animal feeds

These commodities are a shared concern between Health Protection Branch and Agriculture Canada. Information on the use of medicated animal feeds is contained in Agriculture Canada's *Compendium of Medicating Ingredients Brochures*, which specifies the drugs, their dosages, and the indications and conditions of use applicable to the manufacture and sale of registered medicated feeds. Only drugs that comply with the Food and Drugs Act and are listed in the *Compendium* are eligible for registration by the Department of Agriculture.

Bibliography

Curran, R.E. 1953. *Canada's Food and Drugs Laws*. Commerce Clearing House Inc, Chicago, Ill.

Food and Drugs Act and Regulations, with Amendments to October 1982.

Health and Welfare Canada. 1974. Investigation of use and reason for use of non-prescription drugs. *Report D. National Purchase Diary*. C. H. and Z Limited, Toronto.

Narcotic Control Act and Regulations, with Amendments to October 1982.

Prepared by Educational Services: Nonprescription drugs (OTC) series folders

Antacids
Cough Remedies
The Laxative Habit
Vitamin Preparations

Pain Relievers for Self Medication — *Dispatch* No. 28
Third Report on Oral Contraceptives — *Dispatch* No. 45
Cosmetic Safety and the Consumer — *Dispatch* No. 40
— Food and Drug Interactions — *Dispatch* No. 50
— Supplementary Information on Medication — *Dispatch* No. 52

Chapter 3
Record Keeping and the Prescription

Prescriptions for all Schedule drugs must be retained by a pharmacist for a minimum of two years. A verbal prescription must be recorded in writing and the pharmacist must be satisfied that the source of the verbal order is legitimate.

Prescriptions for Schedule drugs must include the following information:

- date and number of prescription;
- name and address of person for whom the prescription is written;
- name and quantity of drug specified by the practitioner;
- name of person filling prescription and name of the practitioner who prescribed it;
- directions for use given with the prescription, including the number of times, if any, it can be refilled.

Refills are only permitted on authorization of a practitioner. Each time a prescription is refilled the following information must be recorded on the original prescription or in a suitable patient record system:

- quantity of drug dispensed,
- date of refill,
- name of the person refilling the prescription.

A narcotic prescription may not be refilled — a new and separate prescription from a practitioner is required.

Bibliography

Food and Drug Regulations, with Amendments to October 1982 (Sections C.01.041 — C.01.042).

Chapter 4
New Drugs

Any drug that has not been sold in Canada for sufficient time and in sufficient quantity to establish in Canada its safety and effectiveness under the use or conditions of use recommended is defined as a new drug in the Regulations.

Research

It has been estimated that chemists create or isolate up to 5 000 chemical substances to arrive at one new marketable drug. After isolation and purification, a new compound will be administered either to tissue cultures or to small animals to see whether there are significant physiological or behavioural changes (whole animals) or morphological or biochemical changes (tissue cultures). This indicates that the drug is active and may thus be useful in reversing pathophysiology of diseased states in man or animal. If promising results are obtained for the compound, preclinical animal studies are initiated.

Preclinical Testing

Preclinical animal studies

Initially the nontoxic to lethal dosage ranges of the compound are determined in tests conducted on non-diseased animals of at least three mammalian species (one must be a non-rodent). If the substance seems to be of potential therapeutic value for human use, more detailed studies are undertaken; these may take several years to complete. If results are positive, the manufacturer may then apply to the HPB for permission to conduct a clinical (i.e. human) pharmacology trial by a qualified investigator.

Clinical pharmacology trial

The compound is administered to healthy human volunteers, building gradually to the predicted effective dose to see whether any unpredicted adverse or toxic symptoms occur. At the same time, the manufacturer is assessing the requirements for large-scale production of the compound.

Production methods and quality control procedures must be designed to ensure a relatively pure compound essentially free of contamination and uniform with respect to all quality aspects. The compound must be stable in its dosage form for a reasonable period of time to permit the clinical investigations to proceed. If any of these factors are unfavourable, measures must be taken to improve them before the compound progresses to clinical trials.

Clinical Trials

The manufacturer files a preclinical new drug submission with the Drugs Directorate requesting permission to distribute the drug to named, qualified investigators, for more extensive testing to determine the new drug's dosage, effectiveness, and safety in treating humans or, in the case of veterinary drugs, animals.

The information submitted must include all testing on humans or animals done up to this time.

In the case of a veterinary drug, data must be available to establish that the administration of the drug as recommended, will not result in harmful drug residues in food products obtained from treated animals. In addition, since the method of manufac-

ture may affect the efficacy and safety of a drug, information on the manufacturing methods, standards, and stability of the drug substance and dosage form must be present, so that the product that may eventually be sold to the public has the same composition as that determined to be effective and safe in the clinical trials.

The investigator is subject to comphrehensive regulations because at this point, testing is being carried out on persons or animals with the disease state or condition that the compound is expected to treat; the results are compared with other drugs or methods of treatment used for the same condition. If clinical studies prove that the new drug has therapeutic value, the manufacturer may then file a new drug submission.

The New Drug Submission

Before marketing a new drug, a manufacturer must file a new drug submission with the Branch and receive a notice of compliance.

The new drug submission contains virtually all information known about the drug and results of studies carried out on the drug substance and the dosage forms available. Information about the drug substance includes its proper name, chemical name(s), details of the method of manufacturing and purification; and its physico-chemical, biological, pharmacological, pharmacodynamic, pharmacokinetic and toxicological properties. Information about the dosage form includes quantitative listing of all ingredients used in the formulation, its method of manufacture, packaging, labelling, results of stability tests, therapeutic claims, side effects, as well as details of clinical studies to support the safety and efficacy of the drug. The submissions themselves range in size from a few pages to several hundred volumes. Samples of the market-ready form of the new drug are also received with the submission for possible analytical testing.

Radiopharmaceuticals

Due to the unique nature of radiopharmaceuticals, review of preclinical and new drug submissions as well as drug status submissions are all the responsibility of the Radiation Protection Bureau, Environmental Health Directorate.

Review and Evaluation

All aspects of the submission are critically reviewed by multidisciplinary teams of the Drugs Directorate. The final reviews deal with the wording of the product monograph, which provides all information on the drug and complete prescribing instructions to physicians. When the new drug submission is found satisfactory, the labels are examined and a *notice of compliance* is issued permitting the manufacturer to sell his product.

Marketing Controls

Once a new drug is on the market, controls do not cease. It may remain in a new drug status for a number of years until the Drugs Directorate is confident that sufficient information has been accumulated from its general use to release it from the rigid controls that are applied to all new drugs. The

manufacturer must report any new information he receives concerning side effects or failure on the part of the drug to produce its desired effect. On request, the manufacturer is required to notify the Drugs Directorate about any animal tests that have provided new information. A notice of compliance for a new drug can be suspended; under these circumstances the drug is removed from the market if this is in the interest of public health.

Bibliography

Food and Drug Regulations, with Amendments to October 1982. (Section C.08.001).

Health and Welfare Canada. 1965. *Guide for Completing Preclinical Submissions on Investigational Drugs* (available from HPB, Bureau of Human Prescription Drugs).

Prepared by and available from Educational Services:
The Marketing of a New Drug — *Dispatch* No. 24

Chapter 5
Drug Standards

What is a Standard?

A "typical" standard may include a physical and chemical description of the drug entity, a description of procedures for identification, the permitted pH range, tests for heavy metals, pyrogen and sterility requirements for parenteral preparations, assay methods and procedures, packaging and storage requirements, and any special label instructions for the user of the drug.

Most single-ingredient drugs are manufactured to standards contained in the publications listed in Schedule B to the Food and Drugs Act:

Pharmacopée Française (Ph.F)
Pharmacopoeia Internationalis (Ph.I.)
British Pharmacopoeia (B.P.)
The Pharmacopeia of the United States of America (U.S.P.)
The Canadian Formulary (C.F.)
The British Pharmaceutical Codex (B.P.C.)
The National Formulary (N.F.)

For some special single-ingredient drugs specific requirements are set out in the Regulations.

Drugs listed in Schedule B publications mentioned above, or in the Regulations, are known as *official drugs*.

A *manufacturer's standard* ("house" standard) may be used by a manufacturer for any drug listed in Schedule B publications so long as the most stringent criteria set out for purity and potency in these publications are met.

A *professed standard* applies to any drug for which there is no standard in the Regulations or in any Schedule B publication. Such standards are necessary for many single-ingredient products, including many new drugs, and for most multiple-ingredient products. In the case of the latter, many individual components will have to meet pharmacopoeial standards, but the final product will have to meet the standard established by the manufacturer.

Some Legislated Drug Specifications

- Compressed tablets that are intended to be swallowed whole must disintegrate within 60 minutes, under specified test conditions. This requirement is designed to ensure that the tablet will not pass whole through the digestive system.
- Enteric coated tablets are formulated to release their ingredients in the upper small intestine after passage intact through the stomach. A test ensures that they do not disintegrate in an acid medium such as is found in the stomach, but do so within 60 subsequent minutes in an alkaline medium similar to that of the upper small intestine.
- Safety factors such as sterility and the absence of pyrogens must be assured in parenteral drugs.

Chapter 6
Advertising/Labelling/Packaging

No person shall label, package, treat, process, sell or advertise any drug in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety.
(Subsection 9(1) Food and Drugs Act)

Labelling

The label of a drug product is one of the most important sources of drug information available to the consumer and health professional.

In addition to the commonly understood meaning of "label," any literature accompanying or belonging to a particular drug product is considered to be labelling material. An inner label is that on an immediate container; an outer label is that on the outside of a drug package.

Basic information must appear on the label:

- proper name of a drug or if there is no proper name, the common name;
- name and address of the manufacturer or distributor of the drug;
- lot number (a means by which a drug can be traced in manufacture and identified in distribution);
- quantitative list of medicinal ingredients by their proper or common names;
- DIN or GP number assigned to the drug (see Chapter 8);
- expiration date for certain specified types of products and for all others that do not maintain potency, purity, and physical characteristics for at least three years from date of manufacture;
- net content (on outer label or if there is only one label, on that label);
- adequate directions to promote the wise use of the drug (e.g. purpose and dosage of drug, route of administration, cautions, warnings, contraindications);
- standard to which the drug is manufactured (see Chapter 5).

If there is insufficient space on the inner label to carry all the required information, some of it may be supplied on a package insert. The inner label should refer to the inclusion of a package insert.

Labels of drugs bought on prescription

Provincial legislation usually specifies what must appear on the label of a drug that is sold on prescription. Those involved in prescribing and dispensing the drug are expected to provide the necessary guidance and warnings so that the drug is properly taken. This information may be communicated by the pharmacist and physician verbally or in written form.

Proper name

This is the name assigned the drug in publications listed in Schedule B to the Food and Drugs Act, or in the Regulations. The proper name usually differs from the chemical name, e.g. acetaminophen is the proper name for *N*-acetyl-*p*-aminophenol.

Recommended dosage

To ensure safe and effective use of a drug, all labels must carry a recommended single or daily dosage or dosage range. For some nonprescription drugs this dosage is limited by legislation (Table of Limits of Drug Dosage, C.01.021) and may only be exceeded if the label bears a caution that a physician should be consulted; a reduced dosage must be stated when these drugs are recommended for children.

Net content

This is the net amount of the drug in terms of weight, measure, or number. When A.S.A. is in a dosage form recommended only for children, the package may not contain more than 24 single-doses.

Children and label precautions

- Codeine-containing compounds sold without a prescription must carry the warning not to administer to children except on the advice of a physician.
- A.S.A. must carry a warning on the label that the substance must be kept out of reach of children. A red octagon must be used to call attention to the warning.
- Preparations containing boric acid or sodium borate must caution against administration to infants and children under the age of three years.

Disposable pressurized containers

The label must call attention to the potential hazards inherent in this type of packaging. The statements "container may explode if heated" and "contents under pressure" as well as precautionary statements with regard to the handling of these containers must appear on the label. This symbol accompanied by the word "Caution" must appear on the main panel:

If the contents are flammable then a statement referring to this must appear on the label along with the appropriate symbol designating the degree of flammability, e.g.:

Radiopharmaceuticals

Special outer label requirements for radiopharmaceuticals include a licence number (see Chapter 10), a radiation warning symbol (☢), and the statement "caution — radioactive material."

Storage instructions

These instructions are necessary to

- maintain the potency and to prevent degradation of ingredients,
- protect the user from dangers inherent in the packaging, as in the case of the aerosol container.

e.g.:

- Store at room temperature.
- Keep refrigerated.

Vitamins and minerals

- When certain disease states or deficiencies require a high intake of specified vitamins and minerals, products are permitted to contain more than the maximum level of the nutrient specified in the vitamin and mineral regulations for most nonprescription drugs. Such products must be clearly labelled "for therapeutic use only" and should be used only on the advice of a physician.
- Labels of all vitamin preparations must carry an expiry date.

Veterinary drugs

- Labels of drugs listed in Part II of Schedule F to the Food and Drug Regulations when sold without a prescription for use in animals must say "for agricultural use only" or "for veterinary use only."
- Labels of most veterinary drugs used in food-producing animals must specify the withdrawal period for the drug (see Chapter 2).

Schedule A diseases

Claims for Schedule A diseases (Appendix I) may not be made on the label except where it is necessary for the safe use of a parenteral (e.g. insulin) or a prescription drug.

Label monitoring

The Drugs Directorate conducts an ongoing monitoring program to assess the manufacturer's compliance with labelling regulations.

Advertising

For the following classes of drugs, professional advice is required for the proper diagnosis and treatment of a disease or condition, or for the administration of the drug. Thus advertising to the *general public* is prohibited for:

- narcotic drugs;
- controlled drugs;
- drugs in Part I of Schedule F (to the Regulations), i.e. prescription drugs for human use except for name, price, and quantity;
- nonprescription drugs that have limits for recommended dosages (as specified in the Table of Limits of Drug Dosage, C.01.021) when these limits are exceeded, e.g. A.S.A. in amounts greater than 975 mg/single dose or 2.925 g/day except for name, price and quantity;

- drugs for treatment of Schedule A diseases (Appendix I);
- vitamins labelled "for therapeutic use only";
- minerals labelled "for therapeutic use only" except for name, price and quantity;

Health professionals and drug advertising

The above restrictions have been developed for the protection of the lay public. They do not apply to advertising directed to health professionals. Such factors as new developments in the field of medicine and treatments for Schedule A diseases are valuable to medical practitioners and of assistance to them in assessing the risk/benefit ratio of treatments.

"False, misleading or deceptive or is likely to create an erroneous impression"

Subsection 9(1) Food and Drugs Act

The above is interpreted to be advertising that

- contradicts current medical or scientific knowledge,
- cannot be supported by clinically valid and statistically reliable data,
- contains confusing or misleading words and phrases,
- gives an overall inaccurate impression.

Some words that may be misleading:

- natural, natural source, natural action
  few drugs are so devoid of processing as to justify the description "natural"; drugs of vegetable origin obtained with minimum processing may be described as "natural source"; "natural action" should not be used as all drugs act by artificially stimulating or assisting bodily functions.
- organic
  no meaning, as many drugs may be defined chemically as organic compounds.

Some unacceptable promotion methods:

- product endorsements
  including professional endorsements, quotations from the media, seals or certificates of approval and testimonials.
- comparisons
  these are often incomplete in that they frequently highlight only the advantages of the advertised product and the disadvantages of the competitor's product; they often emphasize product differences which have little or no significance.
- negative statements
  to say a particular product is non-toxic implies that comparable products may be toxic.
- scientific or technical references
  the consuming public does not generally have sufficient expertise to assess the validity of such references.

Children and drug advertising

Drug advertising should not be directed towards children, as this may

encourage unsupervised use of drugs by children and could establish drug-taking habits early in life. Therefore, drug advertisements such as the following are unacceptable:

- those that portray children discussing drug products or requesting a certain drug;
- those that place more stress on a premium being offered than on the health reason for taking a drug;
- those that exaggerate aspects of a product that would appeal to children, e.g. by portraying drug taking as fun or grown-up;
- those that promote children's drug products by using nationally known persons or characters, e.g. cartoon characters, in the direct presentation of the product.

Preclearance of advertising

All drug advertisements presented on radio and television must be precleared by the Drugs Directorate. This requirement originates with the Broadcasting Regulations administered by the Canadian Radio-Television and Telecommunications Commission.

Advertisements directed to the general public and appearing in newspapers, magazines, and direct mail pieces are not subject to preclearance. They are, however, monitored on a continuing basis and are subject to the same type of legislative controls as are commercials used for broadcast. At the discretion of the manufacturer, the Directorate's opinion may be sought on print advertising material before it is used.

Advertisements directed to health professions in Canadian journals and direct mail pieces are subject to preclearance by the Pharmaceutical Advertising Advisory Board (P.A.A.B.), a non-governmental Board with representation from various professional and manufacturers' associations. The Health Protection Branch is consulted in an advisory capacity. Although the Branch is in agreement with the objectives of this outside Board, the Branch maintains the right under law to disagree with material directed to the health professions in Canada and to take appropriate action.

Packaging

Package requirements are derived in response to the various chemical and physical characteristics of the products they contain. Packages are designed to maintain the potency and purity of a drug for as long as possible. The package itself must not interact with the drug chemically.

Some examples of specialized drug packaging:

- A light-resistant container is needed for phenothiazine tranquilizers because light will diminish their potency and shelf life.
- A glass container is needed for nitroglycerin tablets, as the potency of these tablets will diminish if stored in a semi-porous plastic container.

Bibliography

Food and Drug Regulations with Amendments to October 1982 (Sections C.01.003-C.01.005).

Health and Welfare Canada. 1974. *HPB Guide for Drug Advertisers* (available from HPB, Bureau of Nonprescription Drugs).

Prepared by and available from Educational Services:

Truth in Drug Advertising — *Dispatch* No. 25

Chapter 7
The Drug Manufacturer

Drug manufacturing calls for meticulous care in all phases of its operation; the responsibility for quality control rests solely with the manufacturer. The government provides legislation and guidelines that establish minimum standard conditions under which drugs should be manufactured, processed, distributed, stored, tested, and packaged. Controls vary depending on the type of product, e.g. topical preparations require fewer controls than vaccines.

Premises and Equipment

- All surfaces must be easily cleaned.
- All processing, testing, finishing, distribution, and storage areas must be clean, sanitary, orderly, and free from waste and debris.
- Only materials and equipment required for the specific operation in progress should be present.
- The physical set-up of operations should be such that one drug does not contaminate another (cross-contamination).
- The equipment must be completely and thoroughly cleaned after each operation to prevent cross-contamination.

Qualifications of Personnel

People in charge of manufacturing and quality control must be trained professionals with a background in such sciences as chemistry, biochemistry or pharmacology.

Raw Materials

These are substances used for the manufacture of a drug product. Each lot of raw material received in the plant must be tested for identity, purity, and potency. Material must be retested if it is subject to change in storage.

Storage

Drugs must be stored under conditions that maintain their potency, e.g. some drugs must be refrigerated.

Master Formula

This is a set of instructions stating in detail the materials, procedures, and precautions required to process and uniformly reproduce a specified quantity of drug product.

Product Testing

A finished product must be tested to ensure it meets its specifications (e.g. identity, potency, purity).

Packaging Materials

Packaging materials (labels, caps, bottles, enclosures, seals, papers, boxes, etc.) must be tested and examined for their suitability for the drug. Precautions must be taken to avoid mislabelling. Strict accounting is required of each label used, including rejects.

Monitoring

- Procedures should be double checked and work orders initialled.
- Accuracy and care should be exercised in weighing, measuring, and mixing components into a batch.

- A product should be easily identified throughout the manufacturing process.

Sample Retention

A sample of each lot or batch of a packaged drug must be kept one year beyond the expiration date or three years after the last date of sale of the lot or batch if no expiration date exists. A sample of each lot or batch of raw material used in the production of a drug must be retained by the person who compounds the raw material into dosage form for two years after the lot or batch of raw material is last used.

Record Keeping

A record must be maintained of all information pertinent to a drug product — information on raw material and finished product testing, packaging material checks, adverse drug reactions, recalls or complaints received, lot and order numbers, and date of distribution of each product from the plant.

Recall System

A manufacturer selling a drug must maintain a system that permits rapid recall of any lot of drug.

Bibliography

Good Manufacturing Practices for Drug Manufacturers and Importers may be purchased from:
Supply and Services Canada
Canadian Government Publishing Centre
Ottawa, Canada K1A 0S9

Good Manufacturing Practices Division of the Food and Drug Regulations (C.02.001-C.02.029). October 1982

Chapter 8
Monitoring Drug Safety and Quality

The Drug Identification Number (DIN/GP)

To facilitate its monitoring programs the Branch must be able to quickly identify all marketed drugs. Before a drug can be sold, a manufacturer or importer must apply for and obtain a *drug identification number*, from the Health Protection Branch. Based on the data provided, the Branch maintains files which include the following information about every product on the market:

- names and addresses of persons or firms that appear on the label;
- name of the drug;
- use or purpose for which the drug is recommended;
- quantitative list of medicinal ingredients, i.e. active ingredients;
- copies of all labelling;
- pharmaceutical form, i.e. capsule, powder, liquid, etc.;
- recommended dosage;
- recommended route of administration;
- quantitative list of colouring agents.

Five characteristics are used to generate the six-digit identification number: the manufacturer, active ingredient, concentrations of active ingredients, route(s) of administration, and pharmaceutical form. This number provides the Branch with an inventory of all drugs on the Canadian market. It is prefixed by "GP" in the case of proprietary medicines and "DIN" for all other drugs.

If a manufacturer has two or more products identical in the five characteristics but differing in brand name or in non-medicinal ingredients (e.g. colour), the products would have the same DIN. There are more than 15 000 drug products on record as being sold in Canada.

Who uses the DIN/GP?

- Health Protection Branch,
- provincial governments,
- health insurance companies,
- professional associations,
- poison control information and treatment centres,
- hospitals and universities,
- drug manufacturers.

The Branch relies on the information in applications for DIN/GP for planning and scheduling, and in emergency situations requiring rapid identification of the product.

Since the distribution of radiopharmaceuticals is closely controlled, they are exempt from DIN requirements.

The Inspection

Under the Food and Drugs Act an inspector from HPB's Field Operations Directorate has the authority to enter and inspect a place where drugs are manufactured or stored. His or her task is to monitor compliance with the Act and Regulations. Advice and guidance in interpretation of the legislation may also be offered. The inspector is a trained professional, with qualifications similar to those of persons in charge of quality control in the plant (Chapter 7).

When inspecting a plant, the inspector observes production procedures in a logical sequence from receipt of components into the plant until the product is in a form ready for distribution; the inspection covers the

premises and equipment, sanitation, personnel, quality control, records and samples, product information records, the recall system, and where relevant, special requirements for parenteral drug production. Samples of products may be taken for subsequent examination.

At the end of the inspection, which may take several days, the inspector meets with the manufacturer to discuss the findings and indicates any changes requiring immediate attention. Serious deficiencies may result in prosecution and/or seizure of products.

Imported Drugs

About 18 per cent of the drug products sold in Canada are imported. An importer must maintain comprehensive information to show that the imported drugs are manufactured to specifications and under conditions that meet Canadian requirements. In addition, the following are required:

- The name and address of the drug importer must appear on the label (except for Schedules C and D drugs, where this must appear on the licence application).
- Records must be maintained of the drug distribution in Canada.
- Premises that manufacture Schedules C and D drugs (e.g. insulin, sera, vaccines, radiopharmaceuticals) must be inspected by Health Protection Branch inspectors and licensed before the drug can be imported.

To monitor the technical and scientific competence of foreign pharmaceutical firms and to provide for prompt communication on potential hazards, the Health Protection Branch exchanges information with agencies in other countries, e.g. U.S. Food and Drug Administration.

Analytical Programs

Each regional office of the Branch is equipped with a drug laboratory. Thousands of drugs are tested annually in these laboratories, which have fully qualified staffs comprising chemists, pharmaceutical chemists, microbiologists, and technologists, who are capable of determining such things as a drug's identity, potency, purity, sterility, dissolution rate, and disintegration time.

A specialized facility for national monitoring is located in the Ontario regional laboratory. This unit, the Drug Quality Monitoring Laboratory, is equipped for the automated determination of potency and content uniformity.

What drugs are analyzed?

- Drugs obtained as part of ongoing national monitoring surveys that help to assess the quality of drug products on the Canadian market.
- Drugs (usually controlled, narcotic, or restricted drugs) obtained from illicit channels and submitted by law enforcement agencies for identification (Drug Identification Service).
- Drugs whose quality is questioned by external sources e.g. general public, professional groups.
- Drugs obtained during an inspection, to ensure their com-

pliance with the Act and Regulations.

Drug Quality Assessment Program (QUAD)

The QUAD program was initiated in 1971 to provide pharmacists, physicians, dentists, and other health professionals and purchasing agencies with information about the quality of drugs on the Canadian market. This information is based on the inspection reports and the analyses performed in the regional laboratories. At its inception nearly 400 products, representing 27 drug substances manufactured by 41 firms, were evaluated. Now the program has expanded to include more than 1 600 products, representing over 142 substances manufactured by about 203 firms.

Complaints and Investigations

Investigations are conducted in response to complaints received from various sources outside the Branch. The primary sources of these complaints are consumers and health professionals. The investigation of these complaints begins by focusing attention on how the product has been used and handled by the individual or institution raising the concern. This is to determine whether the complaint has resulted from user, rather than manufacturer, error. When user error has been eliminated as a possible cause, the investigation proceeds to the level of the manufacturer and, where indicated, samples of the drug are analyzed in the Branch's laboratories.

Product complaints should be directed to the nearest regional or district office of the Health Protection Branch.

Drug Adverse Reaction Program

The Canadian Drug Adverse Reaction Program was initiated in 1965

- to assist the Branch in the early detection of adverse drug effects;
- to advise the Branch on drug labelling and advertising with respect to warnings, contraindications, precautions, and adverse effects;
- to inform practitioners of the types and, where possible, the incidence of adverse reactions to drugs;
- to contribute information to the Adverse Reaction Program of the World Health Organization.

The Branch has developed a simple reporting form (Appendix II), familiar to most physicians, which is available on request to the health professions. All reports are handled in strictest confidence. More than 3 000 reports are submitted annually by physicians, nurses, pharmacists, and drug manufacturers.

When a potential problem is identified, the manufacturer(s) is advised. If warranted, the drug may be withdrawn from the market. However, usually only minor changes are required, e.g. a change in prescribing information. Health professionals may be informed of the change by the manufacturer in promotional material or by the Branch in a letter.

Poison Control Program

When this program began in 1957, poison control centres were located in pediatric hospitals because most poisoning cases at that time involved children. Since then, however, the character of the poisoning problem has shifted. The number of adults and adolescents being poisoned has increased. The types of drugs and drug combinations have changed, with more adult poisoning deaths attributed to the use of multiple products (taking excessive amounts of more than one type of drug) and more poisonings with tranquilizers among persons five years of age and older. Also, while the number of accidental poisonings seems to be levelling off, the number of intentional poisonings is increasing.

Today there are more than 300 poison control centres coordinated in a national network. The centres are under the direction of the provincial departments of health, but the collection, coordination, and dissemination of information to the centres is handled by the Health Protection Branch.

Statistics on poisoning cases reported by the centres are computerized and appear annually in *Poison Control Program Statistics*, a Branch publication. The statistics assist the Branch in determining which products need to be more carefully controlled through measures such as ingredient changes, child-resistant packaging, and improvements in labels and warnings.

Ingredient information on over 12 000 products has been entered into a card catalogue system along with treatment advice and has been distributed by the Branch to poison control centres across the country. This enables the centres to respond to enquiries on product ingredients.

The Branch has also published a booklet, *Poisons — Emergency Treatment*. This publication is available to poison control centres and health professionals.

Most telephone directories list an emergency poison control centre number where health professionals and the general public can report a poisoning and obtain immediate advice on what measures to take.

Bibliography

Health and Welfare Canada:

— Published Annually. *Canadian Drug Identification Code* (may be purchased from Supply and Services Canada, Canadian Government Publishing Centre, Ottawa, Canada K1A 0S9).

— 1971. Drug Adverse Reaction Reporting Program. *Rx Bulletin* 2(9): 139-141.

— 1971. FDD's Poison Control Program — A seven-year review. *RX Bulletin* 2(8): 121-128.

— 1971. *Guide for Preparation of Plant Master Files and Imported Drug Submissions* (available from HPB, Bureau of Drug Quality).

— 1973. Poisoning in Canada. *Rx Bulletin* 4(8): 184-185.

— 1980. *Poison Control Program Statistics* (available from HPB, LCDC, Bureau of Epidemiology).

— 1982. *Poisons — Emergency Treatment.* (Available from HPB, LCDC, Bureau of Epidemiology, Product Related Disease Division).

Prepared by and available from Educational Services:

— A Day in the Life of a Drug Inspector — *Dispatch* No. 18
— Protection is our Middle Name — *leaflet*
— How to Lodge a Complaint Effectively — *leaflet.*

Chapter 9
Enforcement/Compliance

Most drug manufacturers and distributors comply with legislation. Thus, the Branch's basic philosophy is one of "voluntary compliance." As a result, when a violation is uncovered, and the matter is not serious, the manufacturer or distributor may be given the opportunity to correct the defect, but under the watchful eye of the Branch's field inspectors. This is often the only action required.

However, when, in the judgment of the Branch, a given situation is a serious one, or after repeated less serious matters have come to the attention of the Branch, it may and does initiate prosecution procedures.

Seizure

An inspector has the power to seize products in violation or suspected to be in violation of legislation. A seizure may be made at the manufacturing, distributing, or retail level and may occur for various reasons, e.g. labelling infractions, unsanitary storage conditions, failure of the drug to meet its standard.

If seized products are found to be in compliance on further analyses or if the manufacturer rectifies the problem, the drugs are released for sale. If the products are not in compliance and the problem is not one that can be corrected by the manufacturer, then the products are destroyed or otherwise disposed of as the Minister directs.

Refused Entry

Imported drugs may be detained or refused entry at the time of importation. If the product defect cannot be corrected, the drugs are denied entry; if the defect can be corrected the importer may be permitted to receive the shipment on condition that correction be made within a specified time.

Recalls

Drug manufacturers receive information concerning product defects from a variety of sources, including the Health Protection Branch. As a result, the manufacturer may initiate a recall of the product. Detailed information relating to the defect and the extent of the recall (distributor or retail level) must be supplied to the Branch. The Branch uses this information and information from its monitoring sources in deciding whether the product defect represents a serious health hazard. If there is a threat to the safety of the consumer, a public alert will be issued through it news media.

In cooperation with the provincial and municipal health agencies and with industry associations, the Branch has established a National Emergency Recall Plan to deal with widespread health hazards to the general public. For example, if a commonly used non-prescription drug was contaminated with strychnine, the Plan would enable the Branch to mobilize many people at different levels of government (federal, provincial, and municipal) to correct the problem. A public alert would also be issued. So far, the Plan has never been implemented in the recall of a drug. Recalls of drugs in the past have not necessitated such mobilization of manpower.

Chapter 10
Biologics, Radiopharmaceuticals

Biologics

These drugs are listed in Schedule D to the Food and Drugs Act. Biologicals are made from living organisms and their products or are synthesized. Examples include insulin, anterior pituitary extracts, sera and vaccines. Because manufacturing of these drugs is intricate and critical to the final product, the premises in which they are manufactured must be inspected and licensed by the Bureau of Biologics before the drug can be sold in Canada. This applies regardless of the country in which the drug is made. The Bureau has its own laboratories for routinely testing these drugs for safety and efficacy.

Note that a drug listed in Schedule D may also be listed in Schedule F to the Regulations. The first schedule regulates how the drug is manufactured; the latter schedule states under what conditions it can be made available to the general public (i.e. via prescription).

Radiopharmaceuticals

These drugs, listed in Schedule C to and Act, emit alpha, beta, or electromagnetic radiations and are used primarily for diagnostic procedures and cancer therapy. Because of their radioactive emissions, careful and exact controls must be implemented in their manufacture and distribution. Thus the same requirements for licensing Schedule D drugs (above) apply also to radiopharmaceuticals.

The Radiation Protection Bureau, Environmental Health Directorate, inspects plants where radiopharmaceuticals are produced and issues the necessary licences. The Bureau has its own laboratories for conducting analyses and research on these drugs. The Radiation Protection Bureau also acts as principal health advisor to the Atomic Energy Control Board, the agency that controls the use of radioactive materials including radiopharmaceuticals.

Bibliography

Food and Drug Regulations with Amendments to October 1982 (Radiopharmaceuticals C.03.201-C.03.209)

Chapter 11
Controlled, Narcotic, and Restricted Drugs

Controlled drugs listed in Schedule G and restricted drugs listed in Schedule H to the Food and Drugs Act, as well as narcotic drugs listed in the Schedule to the Narcotic Control Act (may) have habit-forming properties and are subject to abuse. It is an offence to possess any of these drugs for the purpose of trafficking; moreover, the simple possession of narcotic or restricted drugs for reasons other than those permitted by the Narcotic Control Act or the Food and Drugs Act is also an offence.

To prevent the flow of these drugs from legal to illegal sources, additional controls are imposed on their manufacture, distribution, and sale.

Licensed Dealers

Only dealers licensed by the Department may manufacture, import, or export these drugs; the licensed dealer must maintain detailed records of all transactions for a minimum of two years.

Record Keeping

Records must account for:

- all drugs received, their source, date received;
- all drugs supplied, to whom, date shipped;
- all drugs manufactured, quantity produced, date;
- monthly inventory of all stock on hand.

Pharmacists and physicians must also maintain similar detailed records on all their transactions with controlled and narcotic drugs.

Auditing the Records

Inspectors from the Bureau of Dangerous Drugs, Drugs Directorate, audit the records of licensed dealers, pharmacists, practitioners, and hospitals.

Sale of Narcotic and Controlled Drugs by the Licensed Dealers

With the exception of methadone (used in the treatment of heroin addiction), a licensed dealer may sell these drugs only to another licensed dealer, pharmacist, practitioner, hospital, Regional Director of the Health Protection Branch, or a person authorized by the Minister of the Department of National Health and Welfare to be in possession of such drugs.

Import and Export Controls

For each shipment of these drugs imported into and exported from Canada, a licensed dealer requires a permit that states the source, exact quantities and destination of the shipment and the port of entry or exit.

Single Convention on Narcotic Drugs

The Bureau of Dangerous Drugs maintains a liaison and cooperates with international drug enforcement agencies and foreign government units in areas of mutual interest. It provides quarterly and annual reports and statistics to the International Narcotics Control Board, as required under the 1961 Single Convention on Narcotic Drugs (United Nations).

Chapter 12
Educational Services

All programs of the Health Protection Branch are ultimately directed towards ensuring that the products for which it is responsible are safe and effective when used by the consumer.

To aid the Branch in informing Canadians about food and drug laws and Branch activities, a specialized professional group (the Educational Services Consultants) is attached to the five regional and two district offices of the Branch. They work with the media and with other regional groups such as teachers, community workers, consumer associations, provincial government departments, and professional societies.

The coordinating office of Educational Services is in Ottawa. Here the broad goals of the program are established and resource materials such as booklets, fact sheets, audio-visual aids, and bulletins are generated.

An Educational Services Consultant may be contacted at the following addresses:

Health Protection Branch,
Room 618, Customs Building,
1001 West Pender Street,
VANCOUVER, B.C.
V6E 2M7

Health Protection Branch,
Room 30, Commonwealth Building,
9912-106 Street,
EDMONTON, Alberta
T5K 1C5

Health Protection Branch,
310 Federal Building,
269 Main Street
WINNIPEG, Manitoba
R3C 1B2

Health Protection Branch,
2301 Midland Avenue,
SCARBOROUGH, Ontario
M1P 4R7

Health Protection Branch,
1001 St. Laurent Blvd. West,
LONGUEUIL, Québec
J4K 1C7

Health Protection Branch,
Box 6396,
Station "A",
SAINT JOHN, New Brunswick
E2L 4L9

Health Protection Branch,
Ralston Building,
1557 Hollis Street,
HALIFAX, N.S.
B3J 1V5

Appendix I

Schedule A

No person shall advertise any food, drug, cosmetic or device to the general public as a treatment, preventative or cure for any of the diseases, disorders or abnormal physical states mentioned in Schedule A.
(Subsection 3(1) Food and Drugs Act)

Schedule A, reproduced below, was enacted to prevent advertising claims directed to the general public for serious diseases, disorders, or abnormal physical states, which can only be diagnosed and treated by a medical practitioner, and for diseases with no known cures:

Alcoholism
Alopecia
Anxiety state
Appendicitis
Arteriosclerosis
Arthritis
Bladder disease
Cancer
Convulsions
Depression
Diabetes
Disease of the prostrate
Disorder of menstrual flow
Dysentery
Edematous state
Epilepsy
Gall bladder disease
Gangrene
Glaucoma
Gout
Heart disease
Hernia
Hypertension
Hypotension
Impetigo
Influenza
Kidney disease
Leukemia
Liver disease
Nausea and vomiting of pregnancy
Obesity
Pleurisy
Pneumonia
Poliomyelitis
Rheumatic fever
Scabies
Septicemia
Sexual impotence
Tetanus
Thrombotic and embolic disorders
Thyroid disease
Tuberculosis
Tumor
Ulcer of the gastro-intestinal tract
Vaginitis
Venereal disease

Appendix II

Health and Welfare Canada Santé et Bien-être social Canada

REPORT OF AN ADVERSE REACTION OR EVENT SUSPECTED DUE TO DRUGS, VACCINES*, COSMETICS OR FOOD PRODUCTS

In confidence to Adverse Reaction Program
Product Related Disease Division
Health Protection Branch
Ottawa, Ontario, K1A 0L2

PATIENT DATA

PATIENT'S INITIALS	CHART NUMBER	AGE	SEX	WEIGHT	HEIGHT
			☐ MALE ☐ FEMALE		

ETHNIC ORIGIN

ALLERGIES OR PREVIOUS ADVERSE REACTIONS ☐ NO ☐ YES (*Specify*)

CONDITIONS PRIOR TO REACTION

ADVERSE REACTION OR EVENT

REACTION ONSET WAS ☐ GRADUAL ☐ SUDDEN Specify in min / hrs ☐ OTHER (*Specify*)

DESCRIPTION OF THE ADVERSE REACTION OR EVENT

ONSET OF REACTION Day / Month / Year

LABORATORY VALUES

INTENSITY OF REACTION OR EVENT ☐ MINOR ☐ MODERATE ☐ MAJOR

Hospitalized Because of Reaction ☐ No ☐ Yes

TREATMENT OF REACTION

— SUSPECTED DRUG WAS ☐ STOPPED ☐ DOSE REDUCED ☐ UNCHANGED ☐ OTHER (*Specify*)

— TREATMENT DRUGS OR THERAPY ☐ NO ☐ YES (*Specify*)

OUTCOME OF REACTION ☐ PATIENT RECOVERED ☐ PATIENT RECOVERED WITH RESIDUAL EFFECTS ☐ PATIENT NOT YET RECOVERED ☐ UNKNOWN ☐ FATAL Date and cause

PRODUCT DATA

SUSPECTED DRUGS OR PRODUCTS Trade name / Chemicals / * Batch & Lot No	DATES STARTED	DATES ENDED	DRUG DATA DAILY DOSE	DRUG DATA ROUTE	DRUG DATA REASON FOR USE

DRUGS TAKEN CONCOMITANTLY ☐ YES (*Specify*) ☐ NO

OTHER COMMENTS

HOSPITAL'S NAME

COMPLETED BY

H P B USE ONLY

CITY

PROVINCE

HPB 5069 (11-80) *Use reverse side if necessary* *Français au verso*

Glossary

Addictive	any substance that tends to induce a physiological or psychological dependency
Adulterate	to corrupt, debase, or make impure by the addition of a foreign or inferior substance
Amphetamines	a group of drugs used as stimulants of the central nervous system
Antibiotic	a drug that suppresses the growth of microorganisms in the body and helps control diseases of infectious origin
A.S.A.	acetylsalicylic acid
Assay	laboratory analysis to determine the quantity of one or more substances
Barbiturates	a group of drugs used as sedatives or sleep-inducing agents
B.P.	the British Pharmacopoeia — a series of drug standards
B.P.C.	the British Pharmaceutical Codex — a series of drug standards
C.F.	the Canadian Formulary — a series of drug standards
C.S.D.	Canadian Standard Drugs — a Food and Drugs Act standard assigned to a specific group of drugs
Canada Gazette	a government publication listing all new legislation becoming effective at any given time
Cosmetic	any substance or mixture of substances manufactured, sold, or represented for use in cleansing, altering, or improving the complexion, skin, hair, or teeth, includes deodorants and perfumes
DIN	drug identification number — a six digit, computer-generated number assigned to a specific drug product

Designated Drugs	a group of amphetamine-type stimulant drugs subject to abuse that can only be used in the treatment of designated diseases in humans and animals
Drug	includes any substance or mixture of substances manufactured or sold or represented for use in (a) the diagnosis, treatment, mitigation, or prevention of a disease, disorder, abnormal physical state, or the symptoms thereof, in man or animal; (b) restoring, correcting, or modifying organic functions in man or animal; or (c) disinfection in premises in which food is manufactured, prepared, or kept, or for the control of vermin in such premises
Enteric	a drug specifically coated to pass through the stomach unaltered and disintegrate in the upper intestines
Epidemiology	a science dealing with the incidence, distribution, and control of disease in a population
Epilepsy	a disorder marked by disturbed electrical rhythms of the central nervous system typically manifested by convulsions and clouding of consciousness
Excipient	non-active ingredient in a drug compound
GP	letters preceeding a number assigned to a drug for purposes of identification and registration as a proprietary medicine
Hyperkinetic	abnormally increased and usually purposeless and uncontrollable muscular movement

IU	International Units — a quantity of a biological (as in a vitamin) that produces a particular biological effect — agreed upon as an international standard
Identity	the chemical composition constituting a drug in its given form
LSD	lysergic acid diethylamide — a hallucinogenic drug subject to abuse and therefore available only to institutions involved in highly specialized research
Label	any legend, word, or mark attached to or accompanying a drug or package; an "inner label" is the label on the container; "outer label" is on the package of a drug
Lot number	any combination of letters, figures, or both by which any drug can be traced in manufacture and identified in distribution
N.F.	the National Formulary — a series of drug standards
Narcolepsy	a condition characterized by brief attacks of sleep
Narcotic	a drug that in moderate doses dulls the senses, relieves pain, and induces profound sleep, but has a high potential for addiction leading to abuse
OTCs	nonprescription drugs, frequently called over-the-counter drugs intended for self-medication, and which are generally available in pharmacies only
Ophthalmic	of or relating to the eye

Package	includes anything in which any food, drug, cosmetic, or device is wholly or partly contained, packed, or placed
Parenteral	a drug that is not introduced to the body by means of absorption through the intestinal wall, but by syringe or other instrument
Pathophysiology	the physiology of abnormal states; the functional changes that accompany a particular disease or syndrome
pH	symbol commonly used to measure or indicate the acidity or alkalinity of a solution
Pharmacodynamics	a branch of pharmacology dealing with the reactions between drugs and living structures
Pharmacokinetics	the study of the bodily absorption, distribution, metabolism, and excretion of drugs
Ph.F.	Pharmacopée Française — a set of drug standards
Ph.I.	Pharmacopoeia Internationalis — a set of drug standards
Potency	a measure of the chemical or medicinal effectiveness of a substance
Prescription	an order given by a practitioner, directing that a stated amount of a drug or mixture of drugs specified therein be dispensed for the person named in that order
Proprietary or Patent Medicine Act (PPM)	act of legislation by the Canadian government in 1909 in response to a public concern over patent medicines. Repealed in 1977
Psychotropic	a compound that has the ability to modify mental activity
Purity	the absence of foreign substances in a specific drug
Pyrogen	a fever-producing substance

Residue	a remainder; that which remains after the removal of other substances
Standard	a criterion set up and established by authority as a rule for the measure of quality, weight, value, or quantity
Synthetic	chemical compound built up in a laboratory by the fusing of its various elements; possesses the same molecular structure as its corresponding naturally occurring compound, when there is a naturally occurring compound
U.S.P.	Pharmacopoeia of the United States of America — a set of drug standards

Health Protection and Drug Laws

Health Protection and Drug Laws

Health Protection Branch
Department of National Health and Welfare

Published by authority of the
Minister of National Health and Welfare

Également disponible en français sous le titre
"Les médicaments, la santé et la loi"

1988 Edition

Canadian Cataloguing in Publication Data
Main entry under title:

Health protection and drug laws / Health Protection Branch, Dept. of National Health and Welfare.

Previous ed.: Health Protection Branch, Educational Services, 1983.
Also published in French under title: Les médicaments, la santé et la loi.
Includes bibliographies.
ISBN 0-660-12880-2
DSS cat. no. H49-5/1988E

1. Drugs — Law and legislation — Canada. 2. Canada — Food and Drugs Act. 3. Canada — Narcotic Control Act. I. Canada. Health Protection Branch.

KE3696.H42 1988 344.71/04233 C880970006

Available in Canada through

Associated Bookstores
and other booksellers

or by mail from

Canadian Government Publishing Centre
Supply and Services Canada
Ottawa, Canada K1A 0S9

Catalogue No. H49-5/1988E
ISBN 0-660-12880-2

Price subject to change without notice

Contents

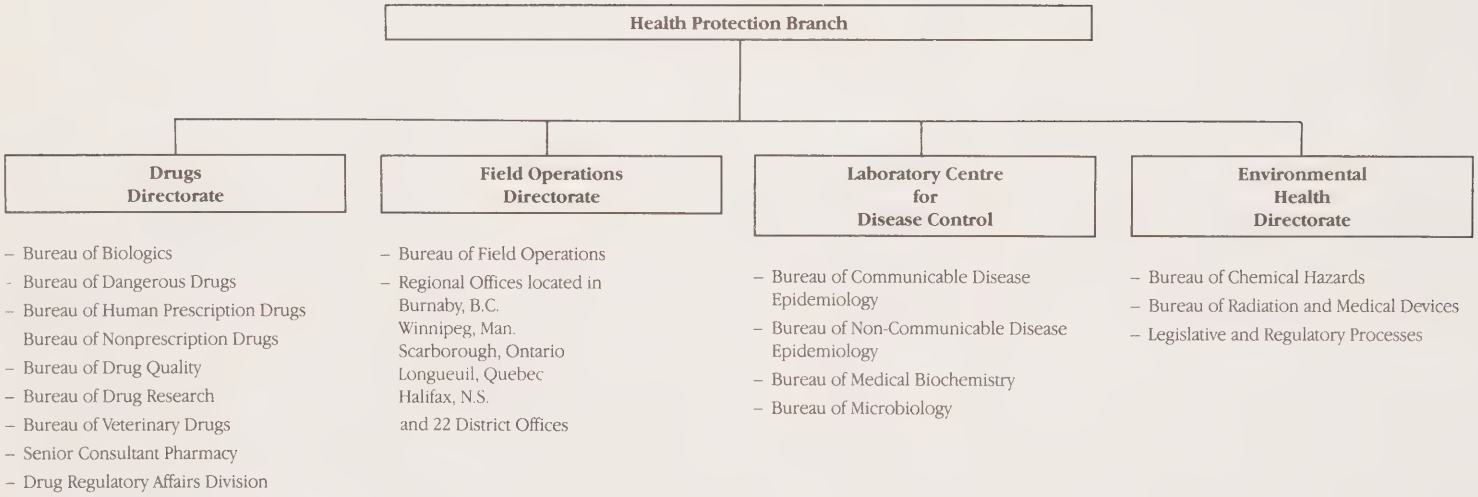
Introduction

Two acts form the basis of the drug laws: the Food and Drugs Act and the Narcotic Control Act. The responsibility for administering these Acts rests mainly with the Health Protection Branch, Department of National Health and Welfare (see the chart reflecting the various drug responsibilities of the Branch.)

Why have drug laws? What are the drug laws? How are these laws implemented? It is the purpose of this publication to answer these three questions. The answers are directed mainly to health professionals, students in the health professions, consumer advocate groups and students of consumer protection laws. It is hoped that this publication will be useful in their dealings with the general public, the government and industry.

Because the volume of legislation that can be outlined in this type of publication is limited, the reader who wants more detail may use this guide in conjunction with the Acts and Regulations and may also refer to the source material listed in the bibliography at the end of each chapter.

A glossary of terms is included at the end of the book.



12/87

Chart reflecting the drug organization of the Health Protection Branch, Health and Welfare Canada, Tunney's Pasture, Ottawa K1A 0L2

Chapter 1

Perspective

Evolution of the Drug Laws

Laws are a means of ensuring that drugs are safe and effective and are being used wisely. The acts that detail these laws, the Food and Drugs Act and the Narcotic Control Act, evolved from different pieces of legislation.

Food and Drugs Act

The Inland Revenue Act of 1876 dealt mostly with the adulteration of alcohol. Actual drugs were not defined. It was the forerunner of more effective legislation such as the Adulteration Act of 1884 which defined what was a drug, adulteration and conditions under which adulteration might take place. It was eventually repealed and the 1920 Food and Drugs Act was invoked. In 1953, the Food and Drugs Act was amended so that it had control of manufacture, distribution and sale of drugs except narcotics. A second piece of legislation was the Proprietary or Patent Medicine Act (PPM) of 1909. It was passed because of concern over efficacy and safety of secret-ingredient drugs. In 1977, this Act was revoked and the drugs formerly listed under it are now governed by the Food and Drugs Act.

Narcotic Control Act

The Opium Act of 1908 prohibited the unauthorized importation and possession of gum or smoking opium. In 1911, it was expanded to the Opium and Drug Act and included other problem drugs, e.g. cocaine and morphine. It was changed again in 1920 to the Opium and Narcotic Control Act because illicit trade in narcotics was increasing and more control was necessary. The Narcotic Control Act (1961) now controls the manufacture, distribution and sale of narcotic drugs.

The Regulations

The Acts contain broad statements relating to safety and efficacy. The more detailed technical requirements are outlined in the Regulations.

The Regulations are also a means of rapidly updating legislation; they have the same force and effect as the Act itself.

Requests for changes arise from many sources: the government, professional or trade organizations, consumer groups and industry. When identifying the need for new or changed regulations, the Health Protection Branch (HPB) considers such subjects as health hazards, fraud, surveillance problems and international standards. Major policy initiatives and regulatory amendments are communicated to the drug industry, health professionals and consumers by means of an Information Letter, distributed by the Branch. Comments submitted by these concerned parties are considered in the drafting of regulatory amendments.

Proposed regulations and the respective Regulatory Impact Analysis Statement (RIAS) are reviewed by the Minister of National Health and Welfare, and if the Minister agrees, are presented to the Governor in Council (a committee of the Cabinet) for prepublication in the Canada Gazette, Part I. Comments received are considered prior to finalizing the amendment for presentation to the Governor in Council for passage into law. When passed, it is published in the Canada Gazette, Part II, which is issued twice monthly and contains all new and amended federal regulations.

Expert Advisory Committees

The assistance of individuals who possess expert knowledge and judgment in specific technical, scientific or medical fields is required by the HPB from time to time to augment the expertise of HPB staff members. Where it is determined that such an Advisory Committee should be established, the Branch publishes an Information Letter stating the Terms of Reference for the Committee. The Committee membership is selected by the Branch after consideration of the nominees.

Branch Communications

The Health Protection Branch (HPB) maintains constant contact with the drug industry and various professional and consumer groups. Such communications are vital for mutual understanding of roles and concerns, and for obtaining the best possible advice in the development of new policies and regulations.

A continuing liaison is maintained with many professional organizations in such fields as pharmacy, medicine, dentistry and veterinary medicine.

The Branch also maintains contact with organizations concerned with specific diseases (e.g. arthritis, cancer, diabetes) and consumer groups through its central office in Ottawa and its five regional offices across Canada.

Bibliography

Morrison, A.B. 1976. The Canadian Approach to Food and Drug Regulations. Food, Drug, Cosmetic Law Journal 30: 632-643.

Material available from the Health Protection Branch:

Canadian Drug Laws and the Consumer – Dispatch No. 33 – Drugs Directorate, Publications.

Protection is our Middle Name – leaflet – Field Operations Directorate, Bureau of Field Operations.

The Canadian Food and Drugs Act and Regulations and the Narcotic Control Act and Regulations may be purchased from:

Supply and Services Canada
Canadian Government Publishing Centre
Ottawa, Canada
K1A 0S9

Chapter 2

Drugs and Their Availability

A drug is any substance used in the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, and in restoring, correcting or modifying organic functions, in man or animals.
(Paraphrased from the Food and Drugs Act)

Availability of drugs is governed by considerations of safety and effectiveness, i.e. the potential for misuse and the amount of professional consultation needed. At one end of the spectrum are drugs such as calamine lotion that may be bought in a grocery store by any person; at the other end are drugs such as LSD (lysergic acid diethylamide) that may be obtained legally only by a research institution with an authorization from the Minister of National Health and Welfare. The former can provide relief from a minor irritation easily self-diagnosed; the latter has no known medicinal use.

Health professionals – physicians, dentists, pharmacists, nurses, veterinarians – play an important role in the availability of drugs to the general public. The extent of their involvement depends on safety considerations. Federal laws provide many of the rules on availability, but provincial pharmacy laws may further restrict the availability of a drug. It is important to note that provincial laws govern the practice of all health professions.

Vaccines, Sera, Radiopharmaceuticals, Antitoxins

Drugs such as these are administered by a physician or a nurse, when required. The patient does not normally have access to these drugs, except through the physician.

Nonprescription Drugs

While it is not possible to categorize these drugs completely, generally speaking, they fall into three groups, and as their name suggests, they may be obtained without a medical prescription. The actual place of sale is regulated by provincial law, usually the Act relating to the practice of pharmacy.

The Proprietary Medicines (or GPs as they are sometimes called) are those which may usually be purchased in any retail outlet. They may be identified by the label which shows a six-digit number preceded by the letters GP. Their use is intended for the symptomatic treatment of minor self-limiting illnesses that do not require the advice or intervention of a health professional. Examples of GPs are some medicated shampoos, cough drops, etc.

The second group also carries a six-digit number on the label, headed, however, by the letters DIN. For the most part, they are available only in pharmacies and are frequently referred to as OTCs (over-the-counter drugs). They too are intended to relieve the symptoms of minor self-limiting illnesses, but for certain of these medicines it is recommended that the advice of a health professional be obtained concerning their use. Examples of these medicines include some laxatives, cough and cold remedies, sinus and/or nasal preparations and many vitamins. Disinfectants are also included in this group.

The third and smallest group are those which should be used only upon consultation with and recommendation by a physician. They are occasionally intended for long-term use. Medicines such as insulin, nitroglycerin, muscle relaxants and antispasmodics are examples of such medicines.

Drug or cosmetic?

Some products may be perceived by the general public to be cosmetics, but because they alter bodily functions they are, by definition, drugs and are regulated as such (all are nonprescription drugs) e.g.:

- A toothpaste is a cosmetic when it cleans, whitens and brightens the teeth; it is a drug when an ingredient, such as fluoride, is added to help prevent tooth decay.
- A deodorant is a cosmetic because it masks odor in perspiration; an antiperspirant is a drug because it suppresses the flow of perspiration.

Federal vs. provincial laws

Some drugs are nonprescription drugs federally but prescription drugs provincially. For example:

British Columbia	ephedrine and its salts (for internal use containing ephedrine as the single active ingredient)
Ontario	digitalis, its glycosides or derivatives.

Prescription Drugs

Many drugs are available to the general public only after consultation with a practitioner (a physician, dentist or veterinarian) and the presentation of a prescription to a pharmacist. A prescription is an order given by a practitioner directing that a stated amount of a drug be dispensed for the person named in the order.

The main reasons for requiring additional control for these drugs are the need for professional direction and supervision in their use and in some cases their potential for abuse or misuse.

Types of prescription drugs are listed below; they are categorized according to the extent of control necessary for their safe use.

Vitamins A and D

Although usually sold as nonprescription drugs, preparations of vitamins A and D for humans require a prescription when the maximum daily dose recommended on the label exceeds 10 000 and 1 000 IU, respectively. Large doses of such vitamins can be toxic.

Schedule F drugs Pr

More than 350 drug substances are listed in Schedule F to the Food and Drug Regulations and represent a wide diversity of classes such as antibiotics, hormones and tranquilizers. Schedule F, perhaps more than any other, is subject to frequent changes. These result from the discovery and introduction to the marketplace of new drug substances, the identification of hazards of certain nonprescription drugs and knowledge of changing abuse and misuse patterns.

The symbol Pr must appear on labels of these drugs.

Controlled drugs 

At present about 14 drugs are classified as controlled drugs and are listed in Schedule G to the Food and Drugs Act. They are stimulants (e.g. amphetamines, methamphetamines) and sedatives (e.g. barbituric acid, methaqualone).

The symbol  must appear on labels and all professional advertisements.

Misuse of the stimulants resulted in their being classed as "designated drugs" that may only be prescribed for the following conditions:

Humans	narcolepsy, hyperkinetic disorders in children, mental retardation (minimal brain dysfunction), epilepsy, parkinsonism, hypotensive states associated with anesthesia
Animals	depression of cardiac and respiratory centres.

Narcotic drugs "N"

Narcotic drugs are controlled by the Narcotic Control Act and Regulations and are listed in the Schedule to that Act. Examples of drugs in this group are cocaine, opium, codeine, morphine, phenyclidine and Cannabis (marihuana).

Some of these drugs have a legitimate medicinal use such as the relief of pain. However, their psychotropic effects (ability to modify mental activity) and addictive properties have led to stringent restrictions on their availability.

The letter "N" must appear on all labels and professional advertisements.

Codeine: the only narcotic preparations that a pharmacist may sell to the general public without a prescription are oral preparations containing 8 mg or its equivalent per tablet of codeine phosphate, or for liquid preparations 20 mg/30 mL or its equivalent of codeine phosphate. (Section 36(1), Narcotic Control Regulations).

Such products must also contain at least two additional medicinal ingredients (e.g. ASA, pheniramine maleate) in specified proportions and should not be administered to children except on the advice of a physician or dentist.

Restricted Drugs

These substances, which have hallucinogenic properties (alter perception from objective reality with serious physiological and psychological effects), have no recognized medicinal use and are dangerous. There are about 29 such chemicals, which are listed in Schedule H to the Food and Drugs Act. The most well known is lysergic acid diethylamide (LSD). These chemicals are only available to institutions involved in highly specialized research. An authorization is required from the Minister of National Health and Welfare before such a drug may be sold.

Veterinary Drugs

Drugs listed in Part I of Schedule F to the Food and Drug Regulations may be sold only on prescription, whether for human or veterinary use. A prescription is not required for drugs listed in Part II, provided they are in a form that can only be used for animals or are labelled (for veterinary use only).

Drug residues in food

Such residues can have serious health consequences in terms of toxicity and allergic responses in sensitive individuals. To minimize this risk, the labels of veterinary drugs used in food-producing animals must specify the withdrawal period, i.e. the time between the last treatment of the drug and the use of the animal for food, either for meat or the collection of milk or eggs. This period must elapse to ensure that residues of the drugs have been eliminated from any edible products derived from the animal. Any antibiotic that leaves traces in the milk of lactating cattle longer than 96 hours after administration must not be used for their treatment.

Medicated animal feeds

The regulation of these commodities is shared between Health Protection Branch and Agriculture Canada. Information on the use of medicated animal feeds is contained in Agriculture Canada's Compendium of Medicating Ingredients brochures, which specifies drugs, dosages, indications and conditions of use applicable to the manufacture and sale of registered medicated feeds. Only drugs that comply with the Food and Drugs Act and are listed in the Compendium are eligible for registration by Agriculture Canada.

Bibliography

Food and Drugs Act and Regulations, with Amendments.

Health and Welfare Canada, 1974. Investigation of use and reason for use of nonprescription drugs. Report D. National Purchase Diary. C. H. and Z Limited, Toronto.

Narcotic Control Act and Regulations, with Amendments.

Material available from the Health Protection Branch, Drugs Directorate, Publications:

Cosmetic Safety and the Consumer – Dispatch No. 40
Food and Drug Interactions – Dispatch No. 50
Drug Interactions – Dispatch No. 56
Analgesics – Dispatch No. 59

Chapter 3

Record Keeping and the Prescription

Prescriptions for all Schedule drugs must be retained by a pharmacist for a minimum of two years. A verbal prescription must be recorded in writing and the pharmacist must be satisfied that the source of the verbal order is legitimate.

Prescriptions for Schedule drugs must include the following information:

- date and number of prescription;
- name and address of person for whom the prescription is written;
- name and quantity of drug specified by the practitioner;
- name of person dispensing the prescription and name of the practitioner who prescribed it;
- directions for use given with the prescription, including the number of times, if any, it can be refilled.

Refills are only permitted on the authorization of a practitioner. Each time a prescription is refilled, the following information must be recorded on the original prescription or in a suitable patient record system:

- quantity of drug dispensed,
- date of refill,
- name of the person dispensing the prescription.

A narcotic prescription may not be refilled – a new and separate prescription from a practitioner is required.

Bibliography

Food and Drugs Act and Regulations, with Amendments (Sections C.01.041 – C.01.042).

Narcotic Control Act and Regulations, with Amendments.

Chapter 4

New Drugs

Any drug that has not been sold in Canada for sufficient time and in sufficient quantity to establish its safety and effectiveness under use or conditions for use recommended is defined as a new drug in the Regulations.

Research

It has been estimated that chemists create or isolate up to 5000 chemical substances to arrive at one new marketable drug. After isolation and purification, a new compound will be administered both to tissue cultures and to a variety of small animals to see whether there are significant physiological or behavioural changes (whole animals) or morphological or biochemical changes in many bodily organs. This indicates that the drug is pharmacologically active and may thus be useful in reversing pathophysiology of diseased states in man or animal. If promising results are obtained for the compound, a whole variety of animal and in vitro tests are completed, including mutagenicity testing, carcinogenicity assays, reproductive studies and effects on the immune system.

Preclinical Testing

Preclinical animal studies

Initially, the nontoxic to lethal dosage ranges of the compound are determined in tests conducted on non-diseased animals of at least three mammalian species (one must be a non-rodent). If the substance seems to possess potentially valuable pharmacological activity, coupled with an acceptable amount of toxicity, the manufacturer may then apply to the HPB for permission to conduct a clinical (i.e. human) pharmacology trial by a qualified investigator.

Clinical pharmacology trial

The compound is administered to healthy human volunteers, building gradually to the predicted effective dose to determine kinetics in man, tolerance and prevalence of adverse effects. At the same time, the manufacturer is assessing the requirements for large-scale production of the compound.

Production methods and quality control procedures must be designed to ensure a relatively pure compound essentially free of contamination and uniform with respect to all quality aspects. The compound must be stable in its dosage form for a reasonable period of time to permit a time-specific clinical investigation to proceed. If any of these factors are unfavourable, measures must be taken to improve them before the compound progresses to clinical trials.

Clinical Trials

The manufacturer files a preclinical new drug submission with the Drugs Directorate requesting permission to distribute the drug to named, qualified investigators, for more extensive clinical testing in patients, to determine the new drug's tolerated dosage, effectiveness and safety for humans or, in the case of veterinary drugs, for animals.

The information submitted must include testing on humans or animals done up to this time. In the case of a veterinary drug, data must be available to establish that the administration of the drug as recommended will not result in harmful drug residues in food products obtained from treated animals.

In addition, since the method of manufacture may affect the efficacy and safety of a drug, information on the manufacturing methods, standards and stability of the drug substance and dosage form must be presented so that the product that may eventually be sold to the public has the same composition as that determined to be effective and safe in the clinical trials.

The investigator is subject to comprehensive regulations because, at this point, testing is being carried out on persons or animals with the disease state or condition that the compound is expected to treat; the results usually compare the new drug with other drugs or older methods of treatment used for the same condition. In many studies a placebo is included in the design to reduce bias. If clinical studies prove that the new drug has therapeutic value, the manufacturer may then file a new drug submission.

The New Drug Submission

Before marketing a new drug, a manufacturer must file a New Drug Submission with the Branch and receive a Notice of Compliance.

The new drug submission contains virtually all information known about the drug and results of preclinical and clinical studies at

several dose strengths and a variety of dosage forms. Information about the drug substance includes its proper name, chemical name(s), details of the method of manufacturing and purification; and its physicochemical, biological, pharmacological, pharmacodynamic, pharmacokinetic and toxicological properties. Information about the dosage form includes quantitative listing of all ingredients used in the formulation, its method of manufacture, packaging, labelling, results of stability tests, therapeutic claims, side effects, as well as details of clinical studies to support the safety and efficacy of the drug. Submissions range in size from a few pages to several hundred volumes. Samples of the market-ready form of the new drug are also received with the submission for possible analytical testing.

Radiopharmaceuticals

Due to the unique nature of radiopharmaceuticals and kits for the preparation of radiopharmaceuticals, review of preclinical and new drug submissions as well as drug status submissions are the responsibility of the Bureau of Radiation and Medical Devices, Environmental Health Directorate.

Review and Evaluation

All aspects of the submission are critically reviewed by multidisciplinary teams of the Drugs Directorate. The final reviews deal with the wording of the product monograph, which provides all information on the drug and complete prescribing instructions for physicians. When the new drug submission is found satisfactory, the labels are examined and a Notice of Compliance is issued permitting the manufacturer to sell the product.

Marketing Controls

Once a new drug is on the market, controls do not cease. It may remain in new drug status for a number of years until the Drugs Directorate is confident that sufficient information on safety and efficacy has been accumulated from its general use to release it from the rigid controls that are applied to all new drugs. The manufacturer must report any new information received concerning serious side effects including failure on the part of the drug to produce its desired effect. On request, the manufacturer is required to notify the Drugs Directorate about any animal tests that have provided new safety information. A Notice of Compliance for a new drug can be suspended; under these circumstances the drug can be removed from the market if it is in the interest of public health.

Bibliography

Food and Drug Regulations, with Amendments. (Section C.08.001).

Health and Welfare Canada, 1984. Chemistry and Manufacturing Guidelines for Preclinical New Drug Submissions (available from Health Protection Branch, Drugs Directorate, Bureau of Human Prescription Drugs).

Health and Welfare Canada, 1985. Guidelines for the Preparation of Drug Submissions on Schedule C Drugs 85-EHD-122 (available from Environmental Health Directorate, Bureau of Radiation and Medical Devices).

Chapter 5

Drug Standards

What Is a Standard?

A "typical" standard may include a physical and chemical description of the drug, a description of procedures for identification, the permitted pH range, tests for heavy metals, pyrogen and sterility requirements for parenteral preparations, assay methods and procedures, packaging and storage requirements, and any special label instructions for the user of the drug.

Most single-ingredient drugs are manufactured to standards contained in the publications listed in Schedule B to the Food and Drugs Act:

Pharmacopée Française (Ph.F)
Pharmacopoeia Internationalis (Ph.I.)
British Pharmacopoeia (B.P.)
The Pharmacopoeia of the United States of America (U.S.P.)
The Canadian Formulary (C.F.)
The British Pharmaceutical Codex (B.P.C.)
The National Formulary (N.F.)

For some special single-ingredient drugs specific requirements are set out in the Regulations.

Drugs listed in Schedule B publications mentioned above, or in the Regulations, are known as official drugs.

A manufacturer's standard ("house" standard) may be used by a manufacturer for any drug listed in Schedule B publications so long as the most stringent criteria set out for purity and potency in these publications are met.

A professed standard applies to any drug for which there is no standard in the Regulations or in any Schedule B publication. Such standards are necessary for some single-ingredient products including

new drugs, and for most multiple-ingredient products. Many raw material components must meet pharmacopoeial standards, but the final product must meet the standard established by the manufacturer, and acceptable to the Branch.

Some Legislated Drug Specifications

- Compressed tablets, except enteric coated tablets, that are intended to be swallowed whole must disintegrate within 60 minutes, under specified test conditions. This requirement is designed to ensure that the tablet will not pass whole through the digestive system.
- Enteric coated tablets are formulated to release their ingredients in the upper small intestine after passing intact through the stomach. A test ensures that they do not disintegrate in an acid medium such as is found in the stomach, but do so within 60 subsequent minutes in an alkaline medium similar to that of the upper small intestine.
- Safety factors such as sterility and the absence of pyrogens must be assured in parenteral drugs.

Chapter 6

Advertising/Labelling/ Packaging

No person shall label, package, treat, process, sell or advertise any drug in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety.

(Subsection 9(1) Food and Drugs Act)

Labelling

The label of a drug product is one of the most important sources of drug information available to the consumer and health professional.

In addition to the commonly understood meaning of "label", any literature accompanying or belonging to a particular drug product is considered to be labelling material. An inner label is that on an immediate container; an outer label is that on the outside of a drug package.

Basic information must appear on the label:

- proper name of a drug or if there is no proper name, the common name;
- name and address of the manufacturer or distributor of the drug;
- lot number (a means by which a drug can be traced in manufacture and identified in distribution);
- quantitative list of medicinal ingredients by their proper or common names;
- DIN or GP number assigned to the drug (see Chapter 8); radiopharmaceuticals are exempted;
- expiration date for certain specified types of products and for all others that do not maintain potency, purity and physical characteristics for at least three years from date of manufacture;

- net content (on outer label or if there is only one label, on that label);
- adequate directions to promote the wise use of the drug (e.g. purpose and dosage of drug, route of administration, cautions, warnings, contraindications);
- standard to which the drug is manufactured (see Chapter 5).

If there is insufficient space on the label to carry all the required information, some of it may be supplied on a package insert. The label should refer to the inclusion of a package insert.

Proper name

This is the name assigned the drug in publications listed in Schedule B to the Food and Drugs Act or in the Regulations. The proper name usually differs from the chemical name, e.g. acetaminophen is the proper name for N-acetyl-p-aminophenol.

Recommended dosage

To ensure safe and effective use of a drug, all labels must carry a recommended single or daily dosage or dosage range. For some nonprescription drugs this dosage is limited by legislation and may only be exceeded if the label states that a physician should be consulted; a reduced dosage must be stated when these drugs are recommended for children. (See Limit Dose Drugs).

Net content

This is the net amount of the drug in terms of weight, measure or number. When ASA is in a dosage form recommended only for children, the package may not contain more than 24 single-doses.

Language of labelling

Directions for use must be in both French and English if the drug is available for sale without prescription in an open self-selection area.

Children and label precautions

Codeine-containing compounds sold without a prescription must carry the warning not to administer to children except on the advice of a physician.

ASA and acetaminophen must carry the following warnings on the label:

- that it should not be administered to a child under two years except on the advice of a physician;
- that it must be kept out of the reach of children;
- that a package containing more than 2 g of ASA or acetaminophen must carry a statement that there is enough drug in the package to seriously harm a child;

- these last two statements must be preceded by a conspicuous symbol such as a red octagon on a white background.

ASA manufacturers have been asked to include a label warning on nonprescription ASA products to the effect that a physician should be consulted before giving such products to children or teenagers with symptoms of flu or chicken pox because of the association with Reye's Syndrome, a rare but serious illness.

A package containing more than 250 mg of iron must carry warning statements that the package must be kept out of the reach of children and that there is enough drug in the package to seriously harm a child; these statements must be preceded by a conspicuous symbol such as a red octagon on a white background.

Preparations containing boric acid or sodium borate must caution against administration to a child under the age of three years.

Child-resistant packaging

In order to reduce the incidence of accidental drug ingestion by children, certain products require a child-resistant package (CRP). These are products containing salicylic acid, its salts and salicylamide; ASA, its salts and derivatives; acetaminophen; liquid preparations containing more than 5% methyl salicylate; and preparations containing more than 250 mg of iron per package. When one of these drugs is recommended solely for children, it must be packaged in a CRP. When the drug is not recommended solely for children, at least one package size must have a child resistant package and all other package sizes must carry a statement on the label that the drug is also available in a child resistant package.

Disposable pressurized containers

The label must call attention to the potential hazards inherent in this type of packaging. The statements "container may explode if heated" and "contents under pressure" as well as precautionary statements with regard to the handling of these containers must appear on the label. This symbol accompanied by the word "Caution" must appear on the main panel.

If the contents are flammable then a statement referring to this must appear on the label along with the appropriate symbol designating the degree of flammability, e.g.:

Radiopharmaceuticals

Special outer label requirements for radiopharmaceuticals include a licence number (see Chapter 10), a radiation warning symbol (☢), and the statement "caution – radioactive material." The licence number is also required on the outer label of kits for the preparation of radiopharmaceuticals.

Storage instructions are necessary to

- maintain the potency and to prevent degradation of ingredients,
- protect the user from dangers inherent in the packaging, as in the case of the aerosol container. For example: – "Store at room temperature" and – "Keep refrigerated."

Vitamins and minerals

- When certain disease states or deficiencies require a high intake of specified vitamins and minerals, products are permitted to contain more than the maximum level of the nutrient specified in the vitamin and mineral regulations for most nonprescription drugs. Such products must be clearly labelled "for therapeutic use only" and should be used only on the advice of a physician.
- Labels of all vitamin preparations must carry an expiry date.

Veterinary drugs

- Labels of drugs listed in Part II of Schedule F to the Food and Drug Regulations when sold without a prescription for use in animals must say "for agricultural use only" or "for veterinary use only."
- Labels of veterinary drugs that create a residue when used in food-producing animals must state the withdrawal period for the drug. This direction ensures that proper use of the drug results in no harmful residue in food derived from treated animals. (See Chapter 2)

Schedule A diseases

Claims for Schedule A diseases (Appendix I) may not be made on the label except where it is necessary for the safe use of a parenteral (e.g. insulin) or a prescription drug.

Label monitoring

The Drugs Directorate conducts an ongoing monitoring program to assess the manufacturer's compliance with labelling regulations.

Labels of drugs sold on prescription

Provincial legislation usually specifies what must appear on the label of a drug that is sold on prescription. Those involved in prescribing and dispensing the drug are expected to provide the necessary guidance and warnings so that the drug is properly taken. This information may be communicated by the pharmacist and physician verbally and/or in written form.

Advertising

For the following classes of drugs, professional advice is required for the proper diagnosis and treatment of a disease or condition, or for the administration of the drug. Thus advertising to the general public is prohibited for:

- narcotic drugs;
- controlled drugs;
- drugs in Part I of Schedule F to the Regulations, i.e. prescription drugs for human use (except for name, price and quantity);
- nonprescription drugs that have limits for recommended dosages (Limit Dose Drugs) when these limits are exceeded, e.g. ASA in amounts greater than 650 mg/single dose or 4.0 g/day (except for name, price and quantity);

- drugs for treatment of Schedule A diseases (Appendix I);
- vitamins labelled "for therapeutic use only" (except for name, price and quantity);
- minerals labelled "for therapeutic use only" (except for name, price and quantity).

Health professionals and drug advertising

The above restrictions have been developed for the protection of the lay public. They do not apply to advertising directed to health professionals. Such factors as new developments in the field of medicine and treatments for Schedule A diseases are valuable to medical practitioners and of assistance to them in assessing the risk/benefit ratio of treatments.

False, misleading or deceptive advertising

"...false, misleading or deceptive or is likely to create an erroneous impression..."

Subsection 9(1) Food and Drugs Act

The above is interpreted to be advertising that

- contradicts current medical or scientific knowledge,
- cannot be supported by clinically valid and statistically reliable data,
- contains confusing or misleading words and phrases,
- gives an overall inaccurate impression.

Some words that may be misleading:

- natural, natural source, natural action
  few drugs are so devoid of processing as to justify the description "natural"; drugs of vegetable origin obtained with minimum processing may be described as "natural source"; "natural action" should not be used as all drugs act by artificially stimulating or assisting bodily functions.
- organic
  has no meaning, as many drugs may be defined chemically as organic compounds.

Some unacceptable promotion methods:

- product endorsements
  including professional endorsements, quotations from the media and seals or certificates of approval.
- comparisons
  these are often incomplete in that they frequently highlight only the advantages of the advertised product and the disadvantages of the competitor's product; they often emphasize product differences that have little or no significance.
- negative statements
  to say a particular product is non-toxic implies that comparable products may be toxic.

- scientific or technical references

  the consuming public does not generally have sufficient expertise to assess the validity of such references.

Children and drug advertising

Drug advertising should not be directed towards children, as this may encourage unsupervised use of drugs by children and could establish drug-taking habits early in life. Therefore, drug advertisements such as the following are unacceptable:

- those that portray children discussing drug products or requesting a certain drug;
- those that place more stress on a premium being offered than on the health reason for taking a drug;
- those that exaggerate aspects of a product that would appeal to children, e.g. by portraying drug taking as fun or grown-up;
- those that promote children's drug products by using nationally known persons or characters, e.g. cartoon characters, in the direct presentation of the product.

Preclearance of advertising

All drug advertisements presented on radio and television must be precleared by the Drugs Directorate. This requirement originates with the Broadcasting Regulations administered by the Canadian Radio-Television and Telecommunications Commission.

Advertisements directed to the general public and appearing in newspapers, magazines, and direct mail pieces are not subject to preclearance. They are, however, monitored on a continuing basis and are subject to the same type of legislative controls as are commercials used for broadcast. Manufacturers may seek the Directorate's opinion on print advertising material before it is used.

Advertisements directed to health professions in Canadian journals and direct mail pieces are subject to preclearance by the Pharmaceutical Advertising Advisory Board (PAAB), a non-governmental Board with representation from various professional and manufacturers' associations. The Health Protection Branch is consulted in an advisory capacity. Although the Branch is in agreement with the objectives of this outside Board, the Branch maintains the right under law to disagree with material directed to the health professions in Canada and to take appropriate action.

Packaging

Package requirements are derived in response to the various chemical and physical characteristics of the products they contain. Packages are designed to maintain the potency and purity of a drug for as long as possible. The package itself must not interact with the drug chemically.

Some examples of specialized drug packaging:

- A light-resistant container is needed for phenothiazine tranquilizers because light reduces their potency and shelf life.
- A glass container is needed for nitroglycerin tablets, as the potency of these tablets will diminish if stored in a semiporous plastic container.
- Child-resistant packaging
- Security packaging

Bibliography

Food and Drug Regulations with Amendments. (Sections C.01.003-C.01.005).

Guide to Consumer Drug Advertising. (Catalogue No. H42-2/3-1984).

Guide for the labelling of drugs for human use. (Catalogue No. H42-2/2-1983).

These publications are available from:

Supply and Services Canada
Canadian Government Publishing Centre
Ottawa, Canada
K1A 0S9

Chapter 7

Good Manufacturing Practices

Meticulous care is required in all phases of the production of drugs for sale in Canada. The government provides legislation that establishes minimum conditions under which drugs should be produced. Guidance on one way of complying with this legislation has been published.

Premises

Buildings should have features that prevent hazards that might affect the quality of the drugs produced therein. These features include suitable environmental conditions, the promotion of good sanitary practices, allowance for adequate cleaning and sanitation, and minimizing the possible contamination of a drug during its production.

Equipment

Equipment should prevent drugs from being contaminated during production from either poor maintenance, misuse or other foreign matter.

Personnel

People are the most important element of any pharmaceutical operation. They should have the right attitude and training to do their job and be supervised in the manufacturing and quality control departments by university graduates or equivalent who have had practical experience in their responsibility area.

Sanitation

A comprehensive sanitation program is essential so that drugs are produced in a plant that maintains a high degree of cleanliness. Employees should always be dressed in suitable clothing, follow good hygienic practices and be subject to a health examination after a prolonged absence from work due to illness.

Raw Materials

Substances that are used in the production of a drug product must always be tested to an acceptable standard before use and subject to retesting if likely to change on storage.

Manufacturing Control

Controls must be exercised during every stage of production to ensure the purity of the drug product from the moment the various raw materials enter the plant until the time the product is released for sale. These controls, at each step of the production process, are the building blocks upon which the quality of the drug product rests. When drugs are produced outside the manufacturer's direct control he must ensure his supplier meets the same high standards. Should these controls for some reason fail, the manufacturer must be able to recall the defective drug effectively and rapidly.

Quality Control

All steps in the production of a drug must be independently approved and audited by professional personnel in the Quality Control Department. It is the responsibility of this group to ensure that all components of the drug product are tested and approved before they are used, and the resulting drug product tested before sale. The combination of the manufacturing and quality controls is often described as Quality Assurance.

Packaging Material Testing

All materials that come in contact with the drug product and all labels must be either tested or examined before being used.

Finished Product Testing

To complement the controls exercised during production, each batch of drug product must undergo "in vitro" testing before it is released for sale. Examples of test requirements are identity, potency,

purity, disintegration plus others in the specification for the drug. In the case of drugs for parenteral use, process validation is also a means to ensure the sterility of the drug in its final container.

Records

Records of all procedures and tests are retained so that a complete history of the production of each lot or batch of a drug product is available for review. These records must be retained for a period of time that exceeds the time that the drug product is sold.

Samples

The manufacturer must retain a sample of each batch of drug produced for a specified period of time.

Stability

Every manufacturer must establish a program to determine how long each drug sold retains its potency and in specific instances add an expiry date to the label.

Sterile Products

Drug products which must be sterile when used require additional precautions during their production and extra controls to ensure they do not become contaminated.

Bibliography

Food and Drug Regulations with Amendments. Good Manufacturing Practices Division. (C.02.001 – C.02.030).

Good Manufacturing Practices for Drug Manufacturers and Importers. Catalogue No. H42 – 2/1 1985.

May be purchased from:

Supply and Services Canada
Canadian Government Publishing Centre
Ottawa, Canada
K1A 0S9

Chapter 8

Drug Safety and Quality

The Drug Identification Number (DIN/GP)

To facilitate its monitoring programs, the Health Protection Branch must be able to identify all marketed drugs quickly. Before a drug can be sold, a manufacturer or importer must apply for and obtain a drug identification number from the Branch. Based on the data provided, the Branch maintains files which include the following information about every product on the market:

- names and addresses of persons or firms that appear on the label;
- name of the drug;
- use or purpose for which the drug is recommended;
- quantitative list of medicinal ingredients, i.e. active ingredients;
- copies of all labelling;
- pharmaceutical form, i.e. capsule, powder, liquid, etc.;
- recommended dosage;
- recommended route of administration;
- quantitative list of colouring agents.

Five characteristics are used to generate the six-digit drug identification number: the manufacturer, active ingredient(s), strength(s) of active ingredient(s), route(s) of administration and pharmaceutical form. This number provides the Branch with an inventory of all drugs on the Canadian market. It is prefixed by "GP" in the case of proprietary medicines and "DIN" for all other drugs.

If a manufacturer has two or more products identical in the five characteristics but differing in brand name or in non-medicinal ingredients (e.g. colour), the products would have the same DIN. There are more than 17 000 drug products on record as being sold in Canada.

Who uses the DIN/GP?

- Health Protection Branch,
- provincial governments,
- health insurance companies,
- health professional associations,
- poison control information and treatment centres,
- hospitals and universities,
- drug manufacturers,
- pharmacies.

The Branch relies on the information in applications for DIN/GP for planning and scheduling, and in emergency situations requiring rapid identification of the product.

Since the distribution of radiopharmaceuticals is more closely controlled and so specialized, they are exempt from DIN requirements.

The Inspection

Under the Food and Drugs Act an inspector from HPB's Field Operations Directorate has the authority to enter and inspect a place where drugs are manufactured or stored. His or her task is to monitor compliance with the Act and Regulations. Advice and guidance in interpretation of the legislation will be offered as needed. The inspector is a trained professional, with qualifications similar to those of persons in charge of quality control in the plant.

When inspecting a plant, the inspector observes production procedures from receipt of components into the plant until the product is in a form ready for distribution. Samples of products may be taken for subsequent examination.

At the end of the inspection, which usually takes several days, the inspector meets with the manufacturer to discuss the findings and indicates any deficiencies requiring immediate attention.

Most drug manufacturers and distributors comply with the legislation. Thus, the Branch's basic philosophy is one of "voluntary compliance." As a result, when a violation is encountered, and the matter is not serious, the manufacturer or distributor may be given the opportunity to correct the defect, with periodic monitoring by the Branch's field inspectors. This is often the only action required.

However, when, in the judgment of the Branch, a given situation is a serious one, or after repeated less serious matters have come to the attention of the Branch, it may and does initiate prosecution procedures.

An inspector also has the power to seize products in violation or suspected to be in violation of legislation. A seizure may be made at the manufacturing, distributing, or retail level and may occur for various reasons, e.g. failure of the drug to meet its standard, lack of sterility, labelling infractions, unsanitary storage conditions.

Analytical Programs

The Branch regional offices in Scarborough, Longueuil and Burnaby are equipped with a drug laboratory for testing of marketed drugs. Drugs are tested annually in these laboratories, which have fully qualified staffs comprising chemists, pharmaceutical chemists, microbiologists and technologists. A drug's identity, potency, content uniformity, purity, sterility, dissolution rate and disintegration time can be determined in these facilities.

Specialized facilities for national monitoring are located in the Ontario and Quebec regional laboratories. These units, the Drug Quality Monitoring Laboratories, are equipped for the automated determination of potency and content uniformity.

Which drugs are analyzed?

- Drugs obtained as part of ongoing national monitoring surveys that help to assess the quality of drug products on the Canadian market.
- Drugs (usually controlled, narcotic or restricted drugs) obtained from illicit channels and submitted by law enforcement agencies for identification (Drug Identification Service).
- Drugs whose quality is questioned by external sources, e.g. general public, professional groups.
- Drugs obtained during an inspection, to ensure their compliance with the Act and Regulations.

Imported Drugs

About 18 percent of the drug products sold in Canada are imported. An importer must maintain comprehensive information to show that the imported drugs are manufactured to specifications and under conditions that meet Canadian requirements. In addition, the following are required:

- The name and address of the drug importer must appear on the label (except for Schedules C and D drugs, where this must appear on the licence application).
- Premises that manufacture Schedules C and D drugs (e.g. insulin, sera, vaccines, radiopharmaceuticals) must be inspected by Health Protection Branch inspectors and licensed before the drug can be imported.

To monitor the technical and scientific competence of foreign pharmaceutical firms and to provide for prompt communication on potential hazards, the Health Protection Branch exchanges information with agencies in other countries, e.g. U.S. Food and Drug Administration.

Imported drugs may be detained or refused entry at the time of importation. If the product defect cannot be corrected, the drugs are denied entry; if the defect can be corrected, the importer may be permitted to receive the shipment on condition that correction be made within a specified time.

Recalls

Drug manufacturers may receive information concerning product defects from a variety of sources, including the Health Protection Branch. As a result, the manufacturer may initiate or be requested to initiate a product recall. Detailed information relating to the defect and the extent of the recall (distributor or retail level) must be supplied to the Branch. The Branch uses this information and information from other sources in deciding whether the product defect represents a serious health hazard. If there is a threat to the safety of the consumer, a public alert will be issued through the media.

In cooperation with the provincial and municipal health agencies and with industry associations, the Branch has established a National Emergency Recall Plan to deal with widespread health hazards to the general public. For example, if a commonly used nonprescription drug was contaminated with strychnine, the Plan would enable the Branch to mobilize many people at different levels of government (federal, provincial and municipal) to correct the problem. A public alert would also be issued. So far, the Plan has never been implemented in the recall of a drug. Recalls of drugs in the past have not necessitated such mobilization of manpower.

Drugs for Export

Canada participates in the World Health Organization's Certification Scheme for pharmaceutical products moving in international commerce. This program provides information to the importing nation on the quality of drugs manufactured in Canada.

Drug Quality Assessment Program (QUAD)

The QUAD program was initiated in 1971 to provide pharmacists, physicians, dentists and other health professionals and purchasing agencies with information about the quality of drugs on the Canadian market. This information is based on the inspection reports and the analyses performed in the regional laboratories.

The program includes nearly 5 000 products, representing over 800 substances manufactured by about 200 firms. Approximately 1 000 of these products are analyzed each year.

Information is now provided on a regular basis to provincial and territorial departments of health and hospital drug purchasing groups.

Complaints and Investigations

Investigations are conducted in response to complaints received from various sources outside the Branch; the primary sources are consumers, health professionals and companies. The investigation begins by determining how the product has been used and handled by the individual or institution raising the concern. If user error is eliminated as a possible cause, the investigation proceeds to the level of the manufacturer and, where indicated, samples of the drug are analysed in the Branch's laboratories.

Product complaints should be directed to the nearest regional or district office of the Health Protection Branch.

Drug Adverse Reaction Program

The Canadian Drug Adverse Reaction Program was initiated in 1965. This voluntary program seeks:

- to assist the Health Protection Branch in the early detection of adverse drug effects;
- to advise the Branch on drug labelling and advertising with respect to warnings, contraindications, precautions and adverse effects;
- to inform practitioners of the types and, where possible, the incidence of adverse reactions to drugs;
- to contribute information to the Adverse Reaction Program of the World Health Organization.

The Branch has developed a simple reporting form (Appendix II), which is available on request to the health professions. All reports are handled in strictest confidence. More than 6 000 reports are submitted annually by physicians, nurses, pharmacists and drug manufacturers.

When a potential problem is identified, the manufacturer(s) is (are) advised. Changes can include such things as amendments to prescribing information or labelling. If warranted, the drug may be withdrawn from the market. Health professionals may be informed of the change by the manufacturer or by the Branch.

Poison Control Program

When this program began in 1957, poison control centres were located in pediatric hospitals because most poisoning cases at that time involved children. Since then, however, the character of the poisoning problem has shifted. The number of adults and adolescents being poisoned has increased. Approximately 100 000 reports are received annually. The types of drugs and drug combinations have changed, with more adult poisoning deaths attributed to the use of multiple products (taking excessive amounts of more than one type of drug) and more

poisonings with tranquilizers among persons five years of age and older. Also, while the number of accidental poisonings seems to be levelling off, the number of intentional poisonings is increasing.

Today, there are more than 300 poison control centres coordinated in a national network. The centres are under the direction of the provincial departments of health, but the collection, coordination and dissemination of information to the centres is handled by the Health Protection Branch.

Statistics on poisoning cases reported by the centres are computerized and appear annually in Poison Control Program Statistics, a Health Protection Branch publication. These statistics assist the Branch in determining which products need to be more carefully controlled through measures such as ingredient changes, child-resistant packaging and improvements in labels and warnings.

The Branch has also published a booklet, Emergency Treatment of Poisoning. This publication is available to poison control centres and health professionals.

Most telephone directories list an emergency poison control centre number where health professionals and the general public can report a poisoning and obtain immediate advice on what measures to take.

Bibliography

Health and Welfare Canada:

Canadian Drug Identification Code, Cat. No. H42-1-1-1985.

Good Manufacturing Practices for Drug Manufacturers and Importers, Cat. No. H42-2-1-1982. (Both available from Supply and Services Canada, Canadian Government Publishing Centre, Ottawa, Canada, K1A 0S9)

Material available from the Health Protection Branch:

Emergency Treatment of Poisoning, 1985. (Laboratory Centre for Disease Control, Bureau of Epidemiology, Product Related Disease Division).

Guide for Preparation of Plant Master Files and Imported Drug Submissions, 1974. (Drugs Directorate, Bureau of Drug Quality).

HPB Information Letter No. 661, Product Recall Procedures, 1984. (Field Operations Directorate, Bureau of Field Operations).

How to Lodge a Complaint Effectively – leaflet – Field Operations Directorate, Bureau of Field Operations.

Poison Control Program Statistics, 1985. (Laboratory Centre for Disease Control, Bureau of Epidemiology).

Protection is our Middle Name – leaflet – Field Operations Directorate, Bureau of Field Operations.

Chapter 9

Biologics, Radiopharmaceuticals

Biologics

Drugs listed in Schedule D to the Food and Drugs Act are subject to especially rigorous controls. The list includes vaccines, blood derivatives, certain hormones and enzymes extracted from animal tissues or cultures of microorganisms and also drugs produced by modern biotechnology. Since manufacturing of these products is intricate and critical to the final product, the premises in which they are manufactured must be inspected and licensed by the Bureau of Biologics before they can be sold in Canada. The Bureau has its own laboratories and routinely tests virtually every lot of every licensed product before permitting them to be distributed for sale.

The regulatory requirements for drugs listed in Schedule D exceed those for other products and constitute the most rigorous of controls on safety and effectiveness of all drugs in Canada.

A drug listed in Schedule D may also be listed in Schedule F to the Regulations. The first schedule regulates how the drug is manufactured; the latter schedule requires that it can be made available to the general public only on prescription.

Radiopharmaceuticals

These drugs, listed in Schedule C to the Act, emit alpha, beta or electromagnetic radiations. Also included in Schedule C are kits for the preparation of radiopharmaceuticals. Radiopharmaceuticals are used primarily for diagnostic procedures and cancer therapy. Because they are radioactive, careful and exact controls must be implemented in

their manufacture and distribution. Thus the same requirements for licensing Schedule D drugs (above) apply also to these drugs.

The Bureau of Radiation and Medical Devices, Environmental Health Directorate, inspects plants where Schedule C drugs are produced, reviews new drug submissions and issues the necessary licences. The Bureau has its own laboratories for conducting analyses and research on these drugs. The Bureau of Radiation and Medical Devices also acts as principal health advisor to the Atomic Energy Control Board, the agency that controls the use of radioactive materials including radiopharmaceuticals.

Bibliography

Food and Drug Regulations with Amendments.
(Schedule C – Division 3 and Schedule D – Division 4).

Chapter 10

Controlled, Narcotic and Restricted Drugs

Controlled drugs listed in Schedule G and restricted drugs listed in Schedule H to the Food and Drugs Act, as well as narcotic drugs listed in the Schedule to the Narcotic Control Act (may) have habit-forming properties and are subject to abuse. It is an offence to possess any of these drugs for the purpose of trafficking; moreover, the simple possession of narcotic or restricted drugs for reasons other than those permitted by the Narcotic Control Act or the Food and Drugs Act is also an offence.

To prevent the flow of these drugs from legal to illegal sources, additional controls are imposed on their manufacture, distribution and sale.

Licensed Dealers

Only dealers licensed by the Department may manufacture, import or export these drugs; the licensed dealer must maintain detailed records of all transactions for a minimum of two years.

Record Keeping

Records must account for:

- all drugs received, their source, date received;
- all drugs supplied, to whom, date shipped;
- all drugs manufactured, quantity produced, date;
- monthly inventory of all stock on hand.

Pharmacists and practitioners must also maintain similar detailed records on all their transactions with controlled and narcotic drugs.

Auditing the Records

Inspectors from the Bureau of Dangerous Drugs, Drugs Directorate, audit the records of licensed dealers, pharmacists, practitioners and hospitals.

Sale of Narcotic and Controlled Drugs by the Licensed Dealers

Subject to further restrictions for methadone and heroin, a licensed dealer may sell these drugs only to another licensed dealer, pharmacist, practitioner, hospital, Regional Director of the Health Protection Branch, or a person authorized by the Minister of the Department of National Health and Welfare to be in possession of such drugs.

Import and Export Controls

For each shipment of these drugs imported to and exported from Canada, a licensed dealer requires a permit that states the source, exact quantities and destination of the shipment and the port of entry or exit.

Single Convention on Narcotic Drugs

The Bureau of Dangerous Drugs maintains a liaison and cooperates with international drug enforcement agencies and foreign government units in areas of mutual interest. It provides quarterly and annual reports and statistics to the International Narcotics Control Board, as required under the 1961 Single Convention on Narcotic Drugs (United Nations).

Convention on Psychotropic Drugs

Canada acceded to the U.N. Convention on Psychotropic Substances in June 1987. Accession to the Convention will strengthen the international efforts to combat trafficking in abusive drugs and substances. The Convention will be implemented in a phased-in manner starting with legislative/regulatory amendments followed by extension of departmental programs to carry out the mandate of the Convention.

Chapter 11

Health Protection Branch

All programs of the Health Protection Branch are ultimately directed towards ensuring that the products for which it is responsible are safe and effective when used by the consumer.

To aid the Branch in informing Canadians about food and drug laws and Branch activities, a variety of publications are available from headquarters or from the five regional offices below.

REGIONAL OFFICES

Health Protection Branch
3155 Willingdon Green
BURNABY, B.C.
V5G 4P2

Health Protection Branch
510 Lagimodière Blvd.
WINNIPEG, Manitoba
R2J 3Y1

Health Protection Branch
2301 Midland Avenue
SCARBOROUGH, Ontario
M1P 4R7

Health Protection Branch
1001 St. Laurent Blvd. West
LONGUEUIL, Québec
J4K 1C7

Health Protection Branch
Ralston Building
1557 Hollis Street
HALIFAX, N.S.
B3J 1V5

Appendix I

Schedule A

No person shall advertise any food, drug, cosmetic or device to the general public as a treatment, preventative or cure for any of the diseases, disorders of abnormal physical states mentioned in Schedule A. (Subsection 3(1) Food and Drugs Act)

Schedule A, reproduced below, was enacted to prevent advertising claims directed to the general public for serious diseases, disorders or abnormal physical states, which can only be diagnosed and treated by a medical practitioner, and for diseases with no known cures:

Alcoholism
Alopecia
Anxiety state
Appendicitis
Arteriosclerosis
Arthritis
Bladder disease
Cancer
Convulsions
Depression
Diabetes
Disease of the prostate
Disorder of menstrual flow
Dysentery
Edematous state
Epilepsy
Gall bladder disease
Gangrene
Glaucoma
Gout
Heart disease
Hernia
Hypertension
Hypotension
Impetigo
Influenza
Kidney disease
Leukemia
Liver disease
Nausea and vomiting of pregnancy
Obesity
Pleurisy
Pneumonia
Poliomyelitis
Rheumatic fever
Scabies
Septicemia
Sexual impotence
Tetanus
Thrombotic and embolic disorders
Thyroid disease
Tuberculosis
Tumour
Ulcer of the gastrointestinal tract
Vaginitis
Venereal disease

Appendix II

Health and Welfare Canada Santé et Bien-être social Canada

REPORT OF AN ADVERSE REACTION OR EVENT SUSPECTED DUE TO DRUGS, VACCINES, COSMETICS OR FOOD PRODUCTS

In confidence to Adverse Reaction Program
Product Related Disease Division
Health Protection Branch
Ottawa, Ontario, K1A 0L2

PATIENT DATA

PATIENT'S INITIALS	CHART NUMBER	AGE	SEX ☐ MALE ☐ FEMALE	WEIGHT	HEIGHT
ETHNIC ORIGIN	ALLERGIES OR PREVIOUS ADVERSE REACTIONS ☐ NO ☐ YES *(Specify)*				

CONDITION PRIOR TO REACTION

ADVERSE REACTION OR EVENT

REACTION ONSET WAS ☐ GRADUAL ☐ SUDDEN Specify min./hr ☐ OTHER *(Specify)*

DESCRIPTION OF THE ADVERSE REACTION OR EVENT

ONSET OF REACTION Day / Month / Year

LABORATORY VALUES

INTENSITY OF REACTION OR EVENT ☐ MINOR ☐ MODERATE ☐ MAJOR

Hospitalized Because of Reaction ☐ No ☐ Yes

TREATMENT OF REACTION
— SUSPECTED DRUG WAS ☐ STOPPED ☐ DOSE REDUCED ☐ UNCHANGED ☐ OTHER *(Specify)*
— TREATMENT DRUGS OR THERAPY ☐ NO ☐ YES *(Specify)*

OUTCOME OF REACTION ☐ PATIENT RECOVERED ☐ PATIENT RECOVERED WITH RESIDUAL EFFECTS ☐ PATIENT NOT YET RECOVERED ☐ UNKNOWN ☐ FATAL Date and cause

PRODUCT DATA

SUSPECTED DRUGS OR PRODUCTS Trade name/Chemicals/*Batch & Lot No.	DATES STARTED	DATES ENDED	DRUG DATA DAILY DOSE	DRUG DATA ROUTE	DRUG DATA REASON FOR USE

DRUGS TAKEN CONCOMITANTLY ☐ YES *(Specify)* ☐ NO

OTHER COMMENTS

HOSPITAL'S NAME	COMPLETED BY	H P B USE ONLY
CITY / PROVINCE		

HPB 5069 (11-80) *Use reverse side if necessary*

Glossary

Addictive	any substance that tends to induce a physiological or psychological dependency
Adulterate	to corrupt, debase, or make impure by the addition of a foreign or inferior substance
Amphetamines	a group of x-methylphenethylamine drugs used as stimulants of the central nervous system
Antibiotic	a drug that suppresses the growth of microorganisms in the body and helps control diseases of infectious origin
ASA	acetylsalicylic acid
Assay	laboratory analysis to determine the quantity of one or more substances
Barbiturates	a group of drugs derived from barbituric acid, used as sedatives or sleep-inducing agents
B.P.	the British Pharmacopoeia – a set of drug standards
B.P.C.	the British Pharmaceutical Codex – a set of drug standards
C.F.	the Canadian Formulary – a set of drug standards
C.S.D.	Canadian Standard Drugs – a Food and Drugs Act standard assigned to a specific group of drugs
Canada Gazette	a government publication listing all new legislation becoming effective at any given time

Cosmetic	any substance or mixture of substances manufactured, sold, or represented for use in cleansing, altering, or improving the complexion, skin, hair, or teeth, includes deodorants and perfumes
DIN	drug identification number – a six digit, computer – generated number assigned to a specific drug product
Designated Drugs	a group of amphetamine-type stimulant drugs with abuse potential that are approved for use in the treatment of certain designated diseases in humans and animals
Drug	includes any substance or mixture of substances manufactured, sold or represented for use in (a) the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical state or the symptoms thereof, in man or animal; (b) restoring, correcting or modifying organic functions in man or animal; or (c) disinfection in premises in which food is manufactured, prepared or kept
Enteric coated	a drug specifically coated to pass through the stomach unaltered and disintegrate in the upper intestines
Epidemiology	the study of the relationships of the various factors determining the frequency and distribution of diseases in a population
Epilepsy	a disorder marked by disturbed electrical activity of the central nervous system, typically manifested by convulsions and clouding of consciousness
Excipient	non-medicinal ingredient in a drug product
Expiration date	the earlier of (1) the date until which a drug maintains its labelled potency, purity, a physical characteristic and (2) the date after which the manufacturer recommends that the drug not be used

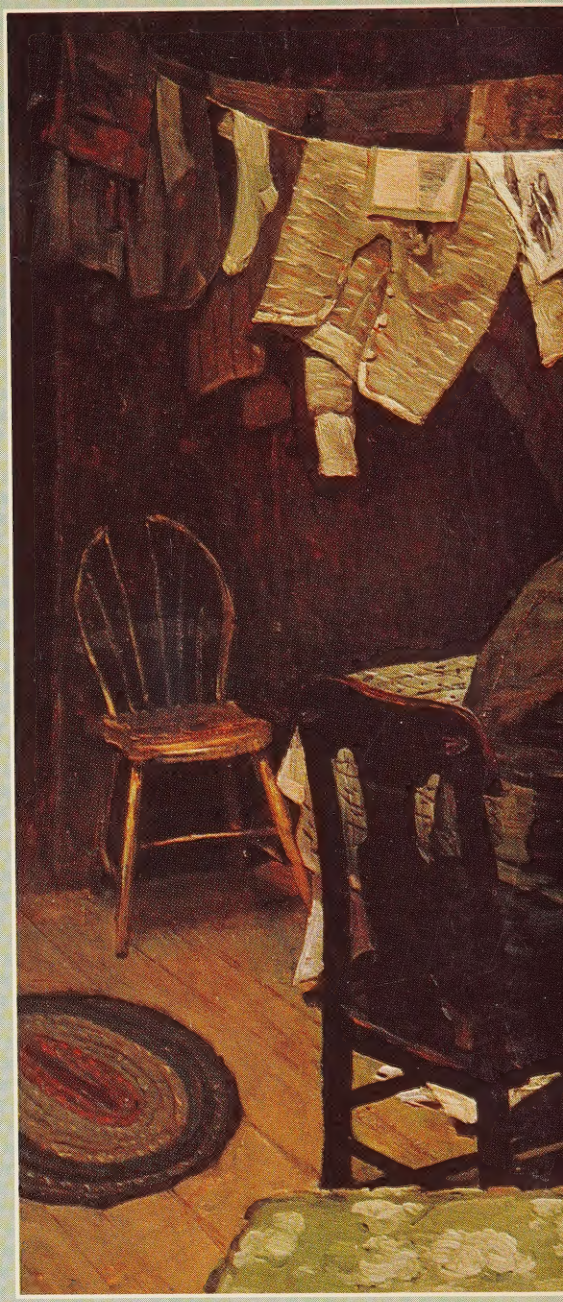
GP	letters preceding a number assigned to a drug for purposes of identification and registration as a proprietary medicine; generally available from many retail outlets
Hyperkinetic	abnormally increased and usually purposeless and uncontrollable muscular movement; "overactive"
IU	International Units – a quantity of a biological (as in a vitamin) that produces a particular biological effect – agreed upon as an international standard
Identity	the chemical composition constituting a drug in its given form
Information letter	an HPB publication intended to inform health professionals, manufacturers and consumer associations, etc. concerned with Branch activities. It may contain proposals or decisions on regulatory change or the comments on a previous regulatory proposal or the reports of Expert Advisory Committees.
LSD	lysergic acid diethylamide – a hallucinogenic drug with no accepted medical use and subject to abuse; legally available only to institutions involved in highly specialized research
Label	any legend, word or mark attached to or accompanying a drug or package; "inner label" is the label on the container; "outer label" is on the package of a drug
Limit Dose Drugs	the Table to Section C.01.021 of the Food and Drug Regulations lists drugs available without prescription but for which maximum single or daily dosages are given. Dosages exceeding these limits are not suitable for self-medication without the advice of a practitioner
Lot number	any combination of letters, figures, or both by which any drug can be traced in manufacture and identified in distribution
N.F.	the National Formulary – a series of drug standards

Narcolepsy	a condition characterized by uncontrolled brief attacks of sleep occurring at intervals throughout the day
Narcotic	a term to describe a drug that in moderate doses dulls the senses, relieves pain and induces sleep, but which has a high potential for addiction and abuse
OTCs	nonprescription drugs, frequently called over-the-counter drugs intended for self-medication, and which are generally available in pharmacies only
Ophthalmic	of or relating to the eye
Package	includes anything in which any drug, cosmetic or device is wholly or partly contained, packed or placed
Parenteral drug	a drug introduced to the body by means other than topical absorption or through the intestinal wall; e.g. intravenous and intramuscular injection
Pathophysiology	the physiology of abnormal states; the functional changes that accompany a particular disease or disorder
pH	a measure of the acidity or alkalinity of a solution
Pharmacodynamics	the study of a branch of pharmacology dealing with the actions of drugs on living organisms, including the correlation of their action with their chemical structure
Pharmacokinetics	the study of the absorption, distribution, metabolism, and excretion of drugs within the body
Ph.F.	Pharmacopée Française – a set of drug standards
Ph.I.	Pharmacopoeia Internationalis – a set of drug standards
Potency	quantitative measure of a medicinal or active ingredient in a product
Practitioner	a person who is registered and entitled under the laws of a province to practice in that province the profession of medicine, dentistry, or veterinary medicine

Prescribing information	information taken from the product monograph and provided to health professionals as part of promotional and advertising material
Prescription	an order given by a practitioner, directing that a stated amount of a drug or mixture of drugs specified therein be dispensed for the person named in that order
Product monograph	factual, scientific document on the drug product, devoid of promotional material, describing the properties, claims, indications and conditions of use of the drug and containing any other information that may be required to provide adequate direction for its safe and effective use
Psychotropic	a compound that has the ability to modify mental activities and affect mood, thinking, perceptions and often behaviour; also known as psychoactive
Purity	the absence of foreign substances in a specific drug
Pyrogen	a fever-producing substance
Residue	a remainder; that which remains after the removal of other substances
Standard	a criterion set up and established by authority as a rule for the measure of quality, weight, value or quantity
Schedule drugs	drugs listed in the Schedule to the Narcotic Control Act or in Schedule G or H of the Food and Drugs Act, or Schedule F of the Food and Drug Regulations
Security package	a package having a security feature that provides reasonable assurance to consumers that the package has not been opened prior to purchase
Synthetic	chemical compound built up in a laboratory by the fusing of its various elements; possesses the same molecular structure as its corresponding naturally occurring compound, when there is a naturally occurring compound

Therapeutic use	drugs (vitamins or minerals) containing this caution are used in the treatment of conditions that the public cannot accurately self-diagnose, i.e. the advice of a practitioner is necessary. Advertising of such products to the general public is restricted to name, price and quantity
U.S.P.	Pharmacopoeia of the United States of America – a set of drug standards
Withdrawal or withholding time (veterinary)	the period of time after drug treatment that a residue remains in animal tissues. Observing this period avoids harmful drug residues remaining in meat, milk or eggs.

Canada



The Sick Child
by M.-A. Suzor-Coté
Collection of the Museum of Quebec
Photo credit: P. Altman